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NEWS 6	FEB 16	New FASTA Display Formats Added to USGENE and PCTGEN
NEWS 7	FEB 16	INPADOCDB and INPAFAMDB Enriched with New Content and Features
NEWS 8	FEB 16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
NEWS 9	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS 10	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS 11	APR 02	DWPI: New display format ALLSTR available
NEWS 12	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS 13	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS 14	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS 15	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
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NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:59:30 ON 17 MAY 2010

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 13:59:47 ON 17 MAY 2010
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STRUCTURE FILE UPDATES: 16 MAY 2010 HIGHEST RN 1224049-79-9
DICTIONARY FILE UPDATES: 16 MAY 2010 HIGHEST RN 1224049-79-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

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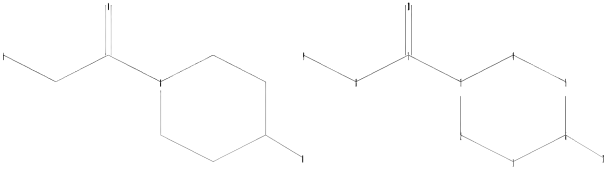
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10579042 A.str



chain nodes :
7 8 9 10 11
ring nodes :

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1  2  3  4  5  6
chain bonds :
3-7  6-11  7-8  7-10  8-9
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  2-3  3-4  3-7  4-5  5-6  6-11  7-10  8-9
exact bonds :
7-8


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS



L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1                STR
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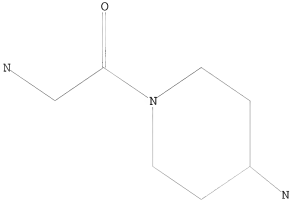


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Structure attributes must be viewed using STN Express query preparation.


=> s l1 sss full
FULL SEARCH INITIATED 14:00:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    53859 TO ITERATE

100.0% PROCESSED    53859 ITERATIONS                          2842 ANSWERS
SEARCH TIME: 00.00.01

L2         2842 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   191.54     191.76

FILE 'CAPLUS' ENTERED AT 14:00:25 ON 17 MAY 2010
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```

FILE COVERS 1907 - 17 May 2010 VOL 152 ISS 21
FILE LAST UPDATED: 16 May 2010 (20100516/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2010

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2010.

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l1
REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 14:00:31 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2691 TO ITERATE

74.3% PROCESSED 2000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 50709 TO 56931
PROJECTED ANSWERS: 1949 TO 3325

L3 50 SEA SSS SAM L1

L4 19 L3

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.50 193.25

FILE 'CAPLUS' ENTERED AT 14:00:43 ON 17 MAY 2010
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FILE COVERS 1907 - 17 May 2010 VOL 152 ISS 21
FILE LAST UPDATED: 16 May 2010 (20100516/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2010

CAplus now includes complete International Patent Classification (IPC)
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=> s l2
L5          227 L2

=> s l5 and py<=2004
      25158169 PY<=2004
L6          102 L5 AND PY<=2004

=> d l ide
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The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
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FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
```

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IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
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OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
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FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):hitstr

L6   ANSWER 1 OF 102  CAPLUS  COPYRIGHT 2010 ACS on STN
IT   220737-64-4     220737-77-9     1071134-10-5
     1071208-15-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (Reductive Aminations of Carbonyl Compds. with Borohydride and Borane
        Reducing Agents)
RN   220737-64-4  CAPLUS
CN   1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[4-[[4-
     (phenylmethoxy)phenyl]amino]-1-piperidinyl]carbonyl]butyl]-  (CA INDEX
     NAME)

Absolute stereochemistry.
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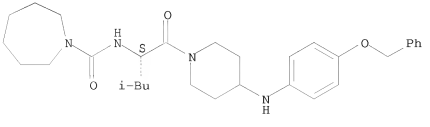


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RN   220737-77-9  CAPLUS
CN   1H-Azepine-1-carboxamide, N-[(1S)-1-[[4-[(4-aminophenyl)(3-
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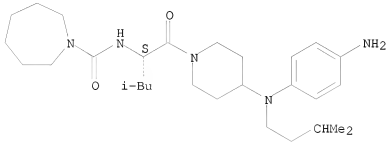
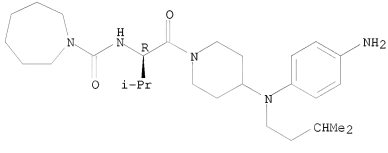
methylbutyl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



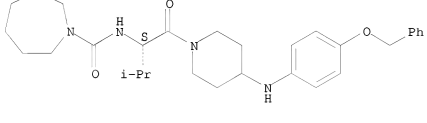
RN 1071134-10-5 CAPLUS
CN 1H-Azepine-1-carboxamide, N-[(1R)-1-[[4-[(4-aminophenyl)(3-methylbutyl)amino]-1-piperidinyl]carbonyl]-2-methylpropyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



RN 1071208-15-5 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-2-methyl-1-[[4-[[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]carbonyl]propyl]- (CA INDEX NAME)

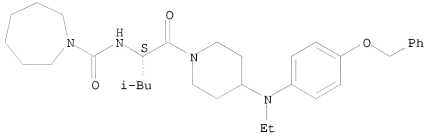
Absolute stereochemistry.



IT 220737-67-7P 220737-84-8P 220737-89-3P
247116-69-4P 1071134-38-7P 1071135-51-7P
1071137-31-9P 1071200-37-7P 1071204-10-8P
1071208-55-3P 1071219-39-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Reductive Aminations of Carbonyl Compds. with Borohydride and Borane Reducing Agents)
RN 220737-67-7 CAPLUS
CN 1H-Azepine-1-carboxamide, N-[(1S)-1-[[4-[ethyl[4-

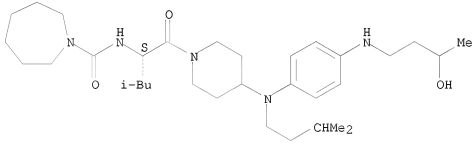
(phenylmethoxy)phenyl]amino]-1-piperidinyl]carbonyl]-3-methylbutyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



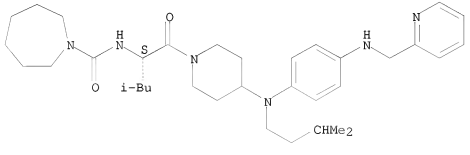
RN 220737-84-8 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-1-[[4-[[4-[(3-hydroxybutyl)amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



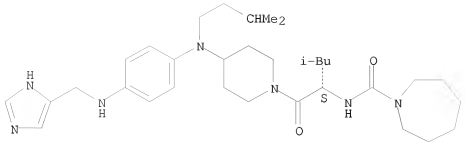
RN 220737-89-3 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[4-[(3-methylbutyl)[4-[(2-pyridinylmethyl)amino]phenyl]amino]-1-piperidinyl]carbonyl]butyl]- (CA INDEX NAME)

Absolute stereochemistry.



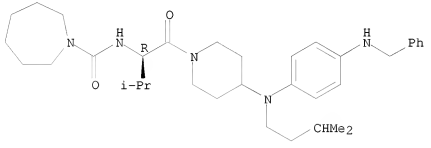
RN 247116-69-4 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-1-[[4-[[4-[(1H-imidazol-5-ylmethyl)amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



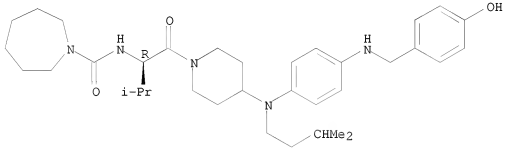
RN 1071134-38-7 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1R)-2-methyl-1-[[4-[(3-methylbutyl)[4-[(phenylmethyl)amino]phenyl]amino]-1-piperidinyl]carbonyl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.



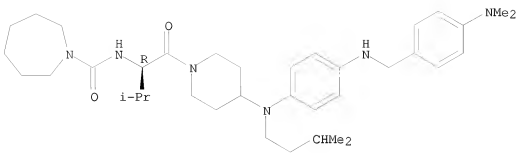
RN 1071135-51-7 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1R)-1-[[4-[[4-[[(4-hydroxyphenyl)methyl]amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-2-methylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



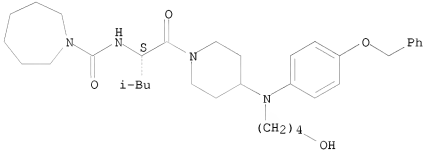
RN 1071137-31-9 CAPLUS
CN 1H-Azepine-1-carboxamide, N-[(1R)-1-[[4-[[4-[[[4-(dimethylamino)phenyl]methyl]amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-2-methylpropyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



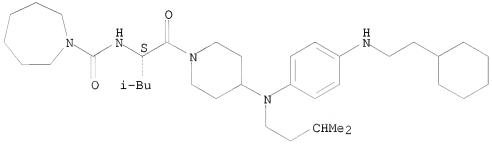
RN 1071200-37-7 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-1-[[4-[(4-hydroxybutyl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



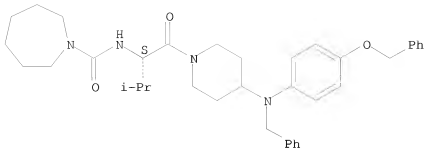
RN 1071204-10-8 CAPLUS
CN 1H-Azepine-1-carboxamide, N-[(1S)-1-[[4-[[4-[(2-cyclohexylethyl)amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



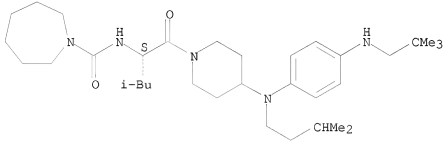
RN 1071208-55-3 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-2-methyl-1-[[4-[[4-(phenylmethoxy)phenyl](phenylmethyl)amino]-1-piperidinyl]carbonyl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 1071219-39-0 CAPLUS
CN 1H-Azepine-1-carboxamide, N-[(1S)-1-[[4-[[4-[(2,2-dimethylpropyl)amino]phenyl](3-methylbutyl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]hexahydro- (CA INDEX NAME)

Absolute stereochemistry.



=> d 2-102 ide
'IDE' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels

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IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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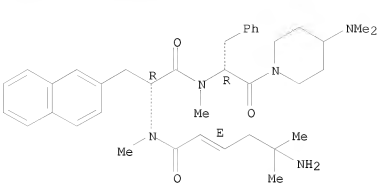
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):abs fhitstr

L6   ANSWER 2 OF 102  CAPLUS  COPYRIGHT 2010 ACS on STN
AB   Peptides R8NH(CR6R7)f(CH2)e-M-(CHR5)d(CH2)cCONR1CH[(CH2)a-G]CONR2CH[(CH2)b-
     J]CO-L [R1 = H, alkyl; L = (un)substituted aza heterocyclyl or aza
     heterocyclylamino or -methylamino; G, J = -O(CH2)kR17 (k = 0-2, R17 = H,
     halo, aryl, hetaryl, alkyl, alkoxy), (un)substituted Ph, pyridyl,
     naphthyl, indolyl, imidazolyl, thienyl, or benzothienyl; a, b, c = 0-2; d,
     f = 0 or 1; e = 0-3; R5-R8 = H or (un)substituted alkyl; M = arylene,
     hetarylene, O, S, or ethylene which is optionally substituted by alkyl,
     arylalkyl, or hetarylalkyl] were prepared for treating medical disorders
     resulting from a deficiency in growth hormone.  Thus,
     (2E)-5-amino-5-methylhex-2-enoic acid
     N-[(1R)-1-[N-[(1R)-1-benzyl-2-[4-[(dimethylamino)methyl]piperidin-1-yl]-2-
     oxoethyl]-N-methylcarbamoyl]-2-(2-naphthyl)ethyl]-N-methylamide was prepared
     via amidation of (2E)-5-[(tert-butoxycarbonyl)amino]-5-methylhex-2-enoic
     acid, followed by cleavage of the protecting group with trifluoroacetic
     acid.
IT   254905-32-3P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of peptide derivs. with growth hormone releasing properties)
RN   254905-32-3  CAPLUS
CN   4-Piperidinamine, 1-[N-[(2E)-5-amino-5-methyl-1-oxo-2-hexen-1-yl]-N-methyl-
     3-(2-naphthalenyl)-D-alanyl-N-methyl-D-phenylalanyl]-N,N-dimethyl-  (CA
     INDEX NAME)
```

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 3 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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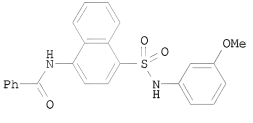


II

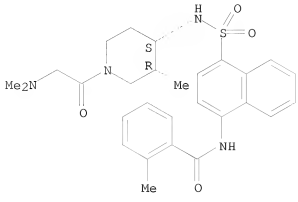
AB The title compds. R1(CH2)mXC(:Z)N(R2)X1ArS(:O)nNR3R4 (I) [Ar = (un)substituted bivalent six-membered aryl group fused to either a six-membered aromatic moiety or to a five- or six-membered nonarom. moiety; R1 = (un)substituted aromatic or nonarom. group; R2 = H, alkyl; R3 = H; R4 = (un)substituted aromatic, nonarom. ring or a bridged bicyclic ring; or NR3R4 = (un)substituted non-aromatic heterocyclyl; X = bond, O, NR5 (R5 = H, alkyl); X1 = bond, carbonyl, (un)substituted methylene; Z = O, NH, S; m = 0-3; n = 1-2] such as II are prepared as inhibitors of the chemokine receptor CCR8 for the treatment of diseases such as asthma, atopic or allergic contact dermatitis, allergic rhinitis, systemic anaphylaxis, rheumatoid arthritis, inflammatory bowel disease, or graft rejection which are mediated by either Th2 cells or eosinophils. Acylation of 4-amino-1-naphthalenesulfonic acid with benzoyl chloride, chlorination of the derived 4-(benzoylamino)-1-naphthalenesulfonic acid pyridine salt with thionyl chloride, and addition of m-anisidine yields II. Ki values for the binding of I to CCR8 are disclosed; for example, II binds to CCCR8 with a Ki value of < 0.5 μM.

IT 1057138-98-3
RL: PRPH (Prophetic)
(Preparation of aryl sulfonamides as inhibitors of the chemokine receptor CCR8 for the treatment of Th2- and eosinophil-mediated diseases)

RN 1057138-98-3 CAPLUS

CN Benzamide, N-[4-[[[(3R,4S)-1-[2-(dimethylamino)acetyl]-3-methyl-4-piperidinyl]amino]sulfonyl]-1-naphthalenyl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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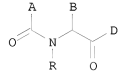

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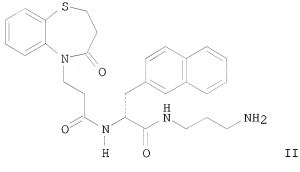


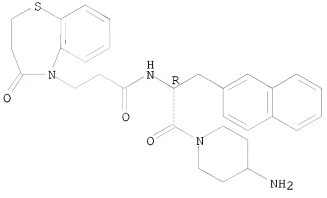
II

AB The invention relates to amino acid derivs. I [A is a lipophilic group including an aliphatic bridging group, B is a lipophilic group, D is a group having at least one (un)substituted amino group, R is H, alkyl or cycloalkyl] and their pharmaceutically acceptable salts and individual isomers which have growth hormone releasing activity in humans or animals and are useful, e.g., in treating osteoporosis, bone fractures, wounds or burns. Thus, a 2-step synthesis afforded amide II.HCl, which showed growth hormone releasing activity < 10-8 M.

IT 220976-80-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-acylated lipophilic amino acid derivs. having growth hormone releasing activity)

RN 220976-80-7 CAPLUS
CN 1,5-Benzothiazepine-5(2H)-propanamide, N-[(1R)-2-(4-amino-1-piperidinyl)-1-(2-naphthalenylmethyl)-2-oxoethyl]-3,4-dihydro-4-oxo-, hydrochloride (1:1) (CA INDEX NAME)

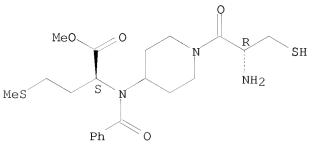
Absolute stereochemistry.



● HCl

L6 ANSWER 5 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB We recently described a novel series of CA1A2X peptidomimetics as farnesyl transferase inhibitors (FTIs). These compds. possess an N-(4-piperidinyl)benzamide scaffold mimicking A1A2 residue. Extensive exploration of structure-activity relationships revealed that replacement of cysteine by substituted benzylimidazoles provided nanomolar FTIs with in vitro activities (18e, IC50 = 4.60 nM on isolated enzyme, EC50 = 20.0 nM for growth inhibition on a tumor cell line). The mol. docking of 18e and 19e in the active site of the enzyme provided details of key interactions with the protein and showed that the methionine or phenylalanine residue fits into the aryl binding site.
IT 755739-00-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperidinyl benzamide derivs. preparation and selective inhibition of farnesyl transferase)
RN 755739-00-5 CAPLUS
CN L-Methionine, N-[1-[(2R)-2-amino-3-mercapto-1-oxopropyl]-4-piperidinyl]-N-benzoyl-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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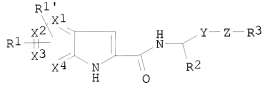

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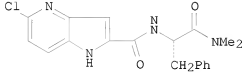


II

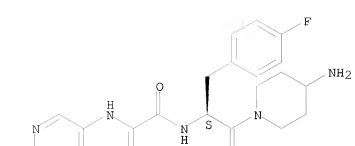
AB Heterocyclyl acyl amino acid derivs. I [one of X1-X4 is N and the others are C; R1, R1' are each independently halo, hydroxy, cyano, alkyl, alkoxy, fluoromethyl, ethenyl or ethynyl; R2 is alkyl or substituted alkyl, carboxy ester or acyl; Y is alkyl or CH(OH); Z is CH2, CO, O, (cyclo)alkylamino or absent, but when Y is CH(OH), Z or R3 must be bonded to Y through a carbon-carbon bond; R3 is H, carbalkoxy, alkoxy, alkyl, arylalkyl, alkylamino, etc.] or their stereoisomers or pharmaceutically-acceptable salts were prepared as inhibitors of glycogen phosphorylase and are useful in the prophylactic or therapeutic treatment of diabetes, hyperglycemia, hypercholesterolemia, hyperinsulinemia, hyperlipidemia, hypertension, atherosclerosis, etc. Thus, pyrrolo[3,2-b]pyridine-2-carboxylic acid L-phenylalaninamide derivative II was prepared via peptide coupling reaction and showed IC50 < 1 mM in the glycogen phosphorylase assay in vitro.

IT 800399-85-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolopyridinecarboxylic acid amide as inhibitors of glycogen phosphorylase)

RN 800399-85-3 CAPLUS

CN 1H-Pyrrolo[2,3-c]pyridine-2-carboxamide, N-[(1S)-2-(4-amino-1-piperidinyl)-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-5-chloro- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 7 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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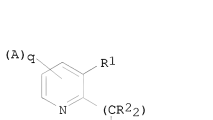

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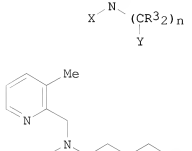


II

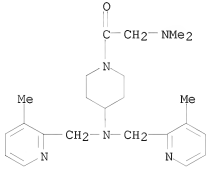
AB Title compds. I [X = (CR32)o-(CR3=CR3)p-(CR32)r-NR52, (CR32)s-R4, (un)substituted mono or bicyclic ring optionally containing N, O or S, etc.; Y = (un)substituted N-containing monocyclic or bicyclic aromatic or partially aromatic moiety; A and R1 = non-interfering substituent provided that two As do not form a ring; R2 and R3 = H or (un)substituted alkyl; R4 = (un)substituted heterocycle or a hetero compound; R5 = H or alkyl; wherein R1 and R2 is not H; and wherein R1 and R2 may be connected to form an addnl. ring if Y does not contain a 2-imidazoyl residue optionally connected to an addnl. ring; q and n independently = 0-4; p = 0-1; o and r independently = 1-4; s = 1-6 provided that if X = (CR3)2-R4, r is at least two if R4 = 2-pyridinyl, quinolinyl, imidazolyl or furan], as well as their pharmaceutically acceptable salts, are prepared and disclosed as having the ability to bind to chemokine receptors, in particular CXCR4. Thus, e.g., II was prepared by reductive amination of {4-[(3-methylpyridin-2-ylmethyl)-amino]-

butyl}carbamic acid tert-Bu ester (preparation given) with 3-benzyloxypyrazine-2-carbaldehyde. The present invention also relates to methods of using such compds., such as in treating HIV infection and inflammatory conditions such as rheumatoid arthritis. In assays to evaluate inhibition of HIV-1, many compds. of the invention exhibited IC50 values in the range of 0.5nM-5μM. Furthermore, the present invention relates to methods to elevate progenitor and stem cell counts, as well as methods to elevate white blood cell counts, using such compds.

IT 780797-43-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyridine derivs. as CXCR4 chemokine receptor binding compds.)

RN 780797-43-5 CAPLUS

CN Ethanone, 1-[4-[bis[(3-methyl-2-pyridinyl)methyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 8 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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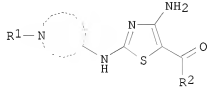

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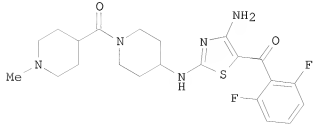


II

AB The title aminothiazole compds. with N-containing cycloalkyl at the 2-amino position [I; N-containing heterocyclyl = (un)substituted N-containing 3-10 membered heterocyclyl; R1 = H, alkyl, alkenyl, alkoxy, etc.; R2 = (un)substituted alkyl, cycloalkyl, alkoxy, aryl, 4-10 membered heterocyclyl] and their pharmaceutically acceptable prodrugs or salts which modulate and/or inhibit the cell proliferation and activity of protein kinases, were prepared Thus, reacting [4-amino-2-(piperidin-4-ylamino)thiazol-5-yl](2,6-difluorophenyl)methanone (preparation given) with 1-methylpiperidine-4-carboxylic acid afforded 65% II which showed Ki of 0.46 μM against CDK2, Ki of 0.13 μM against CDK4, and IC50 of >5 μM in HCT-116 assay for cell growth inhibition. Biol. data were given for over 1100 compds. I. The pharmaceutical compns. comprising the compound I are claimed.

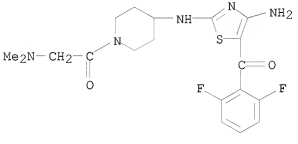
IT 750574-12-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-heterocyclyl-substituted amino-thiazole derivs. as protein kinase inhibitors)

RN 750574-12-0 CAPLUS

CN Ethanone, 1-[4-[[4-amino-5-(2,6-difluorobenzoyl)-2-thiazolyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 9 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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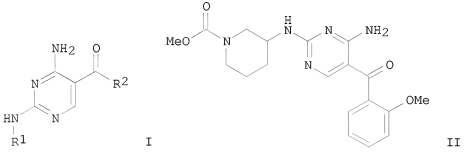


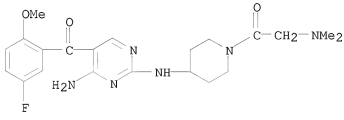
AB The title compds. [I; R1 = (un)substituted heterocyclyl, aryl, cycloalkyl, heteroaryl, alkyl; R2 = (un)substituted aryl, heteroaryl, cycloalkyl, heterocyclyl] which inhibit cyclin-dependent kinases, in particular cyclin-dependent kinase 4 (Cdk4), were prepared and formulated. Thus, reacting [4-amino-2-(piperidin-3-ylamino)pyrimidin-5-yl](2-

methoxyphenyl)methanone as TFA salt (preparation given) with Me chloroformate in the presence of Et3N in CH2Cl2 afforded II which showed IC50 of 0.459 μM against CDK4. In general, the compds. I exhibited cdk4/cyclin D activity with IC50 values and Ki values of <1.0 μM. The compds. I and their pharmaceutically acceptable salts and esters have antiproliferative activity and are useful in the treatment or control of cancer, in particular solid tumors. The antiproliferative potency of some compds. I was tested in the human colon tumor cell line HCT116 with IC50 values of < 30 μM. This invention is also directed to pharmaceutical compns. containing the compds. I, their use for treating or controlling cancer, to a process of their preparation and to intermediates useful in their preparation

IT 741713-16-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (4-aminopyrimidin-5-yl)[(hetero)aryl]methanones as cyclin-dependent kinase inhibitors for treating solid tumors)

RN 741713-16-6 CAPLUS

CN Ethanone, 1-[4-[[4-amino-5-(5-fluoro-2-methoxybenzoyl)-2-pyrimidinyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 10 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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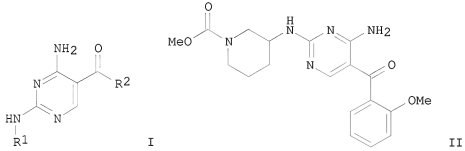


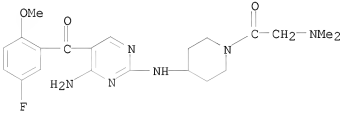
AB The title compds. [I; R1 = (un)substituted heterocyclyl, aryl, cycloalkyl, heteroaryl, alkyl; R2 = (un)substituted aryl, heteroaryl, cycloalkyl, heterocyclyl] which inhibit cyclin-dependent kinases, in particular cyclin-dependent kinase 4 (Cdk4), were prepared and formulated. Thus, reacting [4-amino-2-(piperidin-3-ylamino)pyrimidin-5-yl](2-methoxyphenyl)methanone as TFA salt (preparation given) with Me chloroformate in the presence of Et3N in CH2Cl2 afforded II which showed IC50 of 0.459 μM against CDK4. In general, the compds. I exhibited cdk4/cyclin D activity with IC50 values and Ki values of <1.0 μM. The compds. I and their pharmaceutically acceptable salts and esters have antiproliferative activity and are useful in the treatment or control of cancer, in

particular solid tumors. The antiproliferative potency of some compds. I was tested in the human colon tumor cell line HCT116 with IC50 values of < 30 μM. This invention is also directed to pharmaceutical compns. containing the compds. I, their use for treating or controlling cancer, most particularly the treatment or control of breast, lung, colon and prostate tumors, to a process of their preparation and to intermediates useful in their preparation

IT 741713-16-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (4-aminopyrimidin-5-yl)[(hetero)aryl]methanones as cyclin-dependent kinase inhibitors for treating solid tumors)

RN 741713-16-6 CAPLUS

CN Ethanone, 1-[4-[[4-amino-5-(5-fluoro-2-methoxybenzoyl)-2-pyrimidinyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 11 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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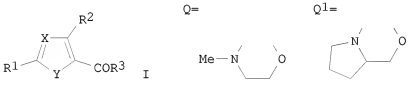


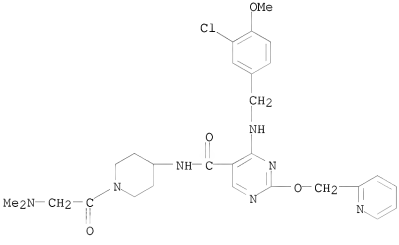
AB The title compds. (I) [X = CH, N; Y = NH, NR, S, O, CH:N, N:CH, N:N, CH:CHC(:R5)N, CH:C(R5), N:C(R7); R1 = each (un)substituted lower alkoxy, amino, heterocyclyl containing N atom(s), HO, or heterocycliloxy containing N atom(s), cyano; R2 = lower alkylamino or lower alkoxy each optionally substituted by an (un)substituted aryl, lower alkoxy group substituted by an aromatic heterocyclic ring containing N atom(s), lower alkylamino group substituted by a (un)substituted heterocyclic ring, (un)substituted arylamino; R3 = each (un)substituted aryl, heterocyclyl containing N atom(s), lower alkyl, lower alkoxy, lower cycloalkoxy, heterocycliloxy containing N atom(s), or NH2; R4-R7 = each (un)substituted aryl, heterocyclyl containing N atom(s), lower alkoxy, or NH2; R4, R5, R6 or R7 may combine with R3 to form a lactone ring Q or Q1; when X = N, Y = CH:N, or N:CH, R2 = an amino group monosubstituted by an (un)substituted arylmethyl, and R3 = (un)substituted lower alkyl, amino monosubstituted by an (un)substituted heterocyclyl-lower alkyl containing N atom(s) in the ring, heterocyclylamino containing N atom(s) in the ring, or (un)substituted lower cycloalkylamino, R1 = each (un)substituted lower alkoxy, amino, heterocycliloxy containing N atom(s) in the ring, or cyano group] or pharmacol. acceptable salts thereof are prepared These compds. have excellent selective PDE V inhibitory activity and therefore, are useful as therapeutic or

prophylactic drugs for treating various diseases due to functional disorders on cGMP-signaling, such as erectile dysfunction, pulmonary hypertension, and diabetic gastroparesis. Thus, 2-(hydroxymethyl)pyridine was treated with NaH in THF and etherified with 2-chloro-5-(3,4,5-trimethoxyphenylcarbonyl)-4-(3-chloro-4-methoxybenzylamino)pyrimidine to give 2-(2-pyridylmethoxy)-5-(3,4,5-trimethoxyphenylcarbonyl)-4-(3-chloro-4-methoxybenzylamino)pyrimidine.

IT 372114-59-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as selective phosphodiesterase V inhibitors for treating various diseases due to functional disorders on cGMP-signaling)

RN 372114-59-5 CAPLUS

CN 5-Pyrimidinecarboxamide, 4-[[(3-chloro-4-methoxyphenyl)methyl]amino]-N-[1-[2-(dimethylamino)acetyl]-4-piperidinyl]-2-(2-pyridinylmethoxy)- (CA INDEX NAME)



L6 ANSWER 12 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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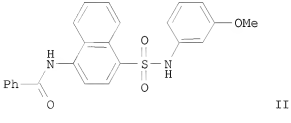


II

AB Compds. R1(CH2)mXYN(R2)X1ArS(:O)nNHR3 (I) [Ar = (un)substituted bivalent six-membered aryl group fused to either a six-membered aromatic moiety or to a five- or six-membered nonarom. moiety; R1 = (un)substituted aromatic or nonarom. group; R2, R4 = H, alkyl, (un)substituted aromatic or nonarom.

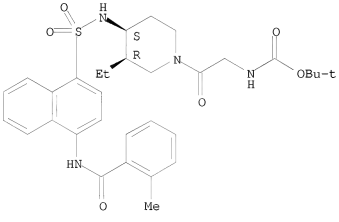
group; R3 = (un)substituted Ph, benzyl, phenethyl, or a non-aromatic ring; X = bond, O, R4N; X1 = bond, carbonyl, (un)substituted methylene; Y = bond, CH2, C(:Z); Z = O, NH, S (if Y = bond then X = bond); m = 0-3; n = 1-2; if X = NR4, R4N(CH2)mR1 may comprise an (un)substituted nonarom. heterocyclic group} such as II are prepared as inhibitors of the chemokine receptor Ccr8 for the treatment of diseases such as asthma, atopic or allergic contact dermatitis, allergic rhinitis, systemic anaphylaxis, rheumatoid arthritis, inflammatory bowel disease, or graft rejection which are mediated by either Th2 cells or eosinophils. Acylation of 4-amino-1-naphthalenesulfonic acid with benzoyl chloride, chlorination of the derived 4-(benzoylamino)-1-naphthalenesulfonic acid pyridine salt with thionyl chloride, and addition of m-anisidine yields II. Ki values for the binding of I to Ccr8 are disclosed; for example, II binds to Ccr8 with a Ki value of < 0.5 μM.

IT 723306-42-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of sulfonamides as inhibitors of the chemokine receptor Ccr8 for the treatment of eosinophil and Th2-mediated diseases such as asthma, allergic dermatitis, and rheumatoid arthritis)

RN 723306-42-1 CAPLUS

CN Carbamic acid, [2-[(3R,4S)-3-ethyl-4-[[[4-[(2-methylbenzoyl)amino]-1-naphthalenyl]sulfonyl]amino]-1-piperidinyl]-2-oxoethyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 13 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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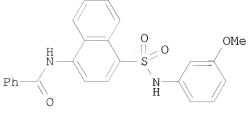


II

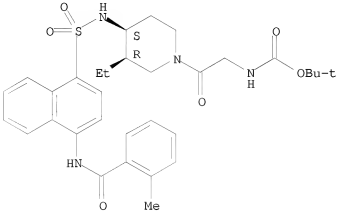
AB Compds. R1(CH2)mXYN(R2)X1ArS(:O)nNHR3 (I) [Ar = (un)substituted bivalent six-membered aryl group fused to either a six-membered aromatic moiety or to a five- or six-membered nonarom. moiety; R1 = (un)substituted aromatic or nonarom. group; R2, R4 = H, alkyl, (un)substituted aromatic or nonarom. group; R3 = (un)substituted Ph, benzyl, phenethyl, or a non-aromatic ring; X = bond, O, R4N; X1 = bond, carbonyl, (un)substituted methylene; Y = bond, CH2, C(:Z); Z = O, NH, S (if Y = bond then X = bond); m = 0-3; n = 1-2; if X = NR4, R4N(CH2)mR1 may comprise an (un)substituted nonarom. heterocyclic group] such as II are prepared as inhibitors of the chemokine receptor Ccr8 for the treatment of diseases such as asthma, atopic or allergic contact dermatitis, allergic rhinitis, systemic anaphylaxis, rheumatoid arthritis, inflammatory bowel disease, or graft rejection which are mediated by either Th2 cells or eosinophils. Acylation of 4-amino-1-naphthalenesulfonic acid with benzoyl chloride, chlorination of the derived 4-(benzoylamino)-1-naphthalenesulfonic acid pyridine salt with thionyl chloride, and addition of m-anisidine yields II. Ki values for the binding of I to Ccr8 are disclosed; for example, II binds to Ccr8 with a Ki value of < 0.5 μM.

IT 723306-42-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of sulfonamides as inhibitors of the chemokine receptor Ccr8 for the treatment of eosinophil and Th2-mediated diseases such as asthma, allergic dermatitis, and rheumatoid arthritis)

RN 723306-42-1 CAPLUS

CN Carbamic acid, [2-[(3R,4S)-3-ethyl-4-[[[4-[(2-methylbenzoyl)amino]-1-naphthalenyl]sulfonyl]amino]-1-piperidinyl]-2-oxoethyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 14 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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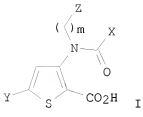


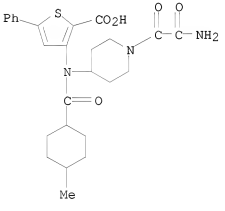
I

AB Title compds. (I; Z = 3-7 membered heterocyclyl, cycloalkyl; X = 3-10 membered cycloalkyl; Y = 6-10 membered aryl; m = 0, 1; when Y = Ph, X ≠ 4-methylcyclohexyl), were prepared Thus, 3-[[(2-carboxy-5-phenylthiophen-3-yl)-(4-methylcyclohexanecarbonyl)amino]methyl]piperidinium trifluoroacetate (preparation from 3-amino-5-phenylthiophene-2-carboxylate, 3-formyl-N-benzyloxycarbonylpiperidine, and trans-4-methylcyclohexanecarbonyl chloride given) inhibited HCV RNA-dependent RNA polymerase with IC50 <5 μM.

IT 712353-19-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of thiophenecarboxylates for the treatment or prevention of flavivirus infections)

RN 712353-19-0 CAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[1-(2-amino-2-oxoacetyl)-4-piperidinyl][(4-methylcyclohexyl)carbonyl]amino]-5-phenyl- (CA INDEX NAME)



L6 ANSWER 15 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = O, S, phenylsulfonylimino, etc.; X = O, S, substituted imino, etc.; Y, Z = alkyl, difluoromethyl, trifluoromethyl, etc.; R1 = 5-7 membered aza, diaza, triaza, etc. heterocycle; R2 = H, phenylmethyl, alkyl, etc.; R3 = H, Ph, pyridinyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For

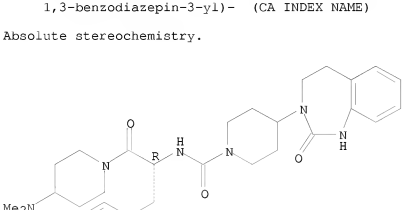
example, benzo-1,3-diazepin-2-one II was prepared from 1-(3,4-diethylphenyl)ethanone in 8-steps. In human CGRP receptor binding affinity assays, compds. I exhibited IC50 values < 10000 nM. Compds. I are claimed useful for the treatment of migraine headaches.

IT 686296-65-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzo-1,3-diazepin-2-ones and related compds. as CGRP receptor antagonists for the treatment of migraine headaches)

RN 686296-65-1 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[(3,4-diethylphenyl)methyl]-2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl]-4-(1,2,4,5-tetrahydro-2-oxo-3H-1,3-benzodiazepin-3-yl)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 16 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = O, S, phenylsulfonylimino, etc.; X = O, S, substituted imino, etc.; U = alkyl, alkenyl, alkynyl, etc.; V = Cl, Br, amino, etc.; W = H, halo, difluoromethyl, etc.; R1 = 5-7 membered aza, diaza, triaza, etc. heterocycle; R2 = H, phenylmethyl, alkyl, etc.; R3 = H, Ph, pyridinyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, benzo-1,3-diazepin-2-one II was prepared from 4-amino-3-chloro-5-trifluoromethylbenzoic acid in 9-steps. In human CGRP receptor binding affinity assays, compds. I exhibited IC50 values < 10000 nM. Compds. I are claimed useful for the treatment of migraine headaches.

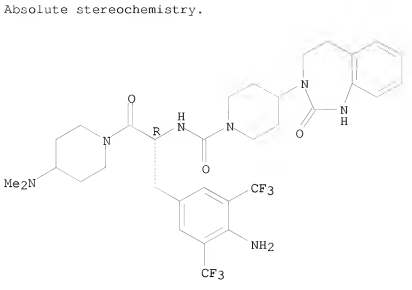
IT 1072606-52-0
RL: PRPH (Prophetic)
(Preparation of benzo-1,3-diazepin-2-ones and related compounds as CGRP receptor antagonists for the treatment of migraine headaches)

RN 1072606-52-0 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[[4-amino-3,5-bis(trifluoromethyl)phenyl]methyl]-2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl]-4-(1,2,4,5-tetrahydro-2-oxo-3H-1,3-benzodiazepin-3-yl)- (CA

INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 17 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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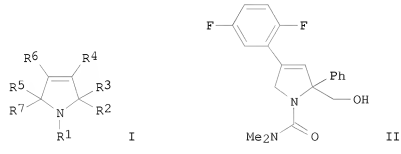


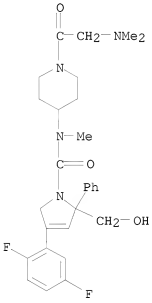
AB Title compds. I [wherein R1 = (un)substituted acyl(alkyl), carbamoyl(alkyl), sulfamoyl(alkyl), aryl, heterocyclyl, alkyl, etc.; R2 and R6 = independently (un)substituted aryl(alkyl), cycloalkyl, or heterocyclyl; R3 = (un)substituted alkoxyalk(en/yn)yl, carbamoylalk(en/yn)yl, alkylsulfonylalk(en/yn)yl, etc.; R4, R5, and R7 = independently H or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, perfluoroalkyl, arylalkyl, or heterocyclyl; or R5 and R7 are combined to form an oxo or sulfoxo; or pharmaceutically acceptable salt of stereoisomer thereof] were prepared for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention is also related to compns. which comprise these compds., and methods of using them to treat cancer (no data). For instance, palladium catalyzed Suzuki coupling of 7a-phenyldihydro-1H-pyrrolo[1,2-c][1,3]oxazole-3,6(5H)-dione (multi-step preparation given) and 2,5-difluorophenylboronic acid afforded 6-(2,5-difluorophenyl)-7a-phenyl-5,7a-dihydro-1H-pyrrolo[1,2-c][1,3]oxazol-3-one. The pyrrolooxazolone was treated with NaOH in EtOH to give the (hydroxymethyl)pyrrole, which was O-protected with tert-butyldimethylsilyl chloride. Reaction of the pyrrole with triphosgene and dimethylamine, followed by deprotection using triethylamine trihydrofluoride in MeCN provided II. In a kinesin ATPase assay using a human KSP motor domain

construct and microtubules from bovine brain tubulin, example compds. inhibited the ATPase hydrolysis reaction with IC50 ≤ 50 μM.

IT 686320-63-8P, 4-(2,5-Difluorophenyl)-N-[1-(N,N-dimethylglycyl)piperidin-4-yl]-2-(hydroxymethyl)-N-methyl-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(KSP inhibitor; preparation of dihydropyrroles as KSP inhibitors for treating proliferative diseases)

RN 686320-63-8 CAPLUS

CN 1H-Pyrrole-1-carboxamide, 4-(2,5-difluorophenyl)-N-[1-[2-(dimethylamino)acetyl]-4-piperidinyl]-2,5-dihydro-2-(hydroxymethyl)-N-methyl-2-phenyl- (CA INDEX NAME)



L6 ANSWER 18 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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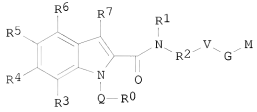
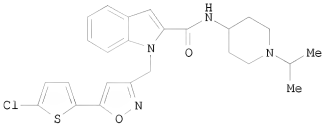


I



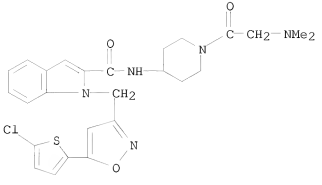
II

AB The title compds. I [wherein R0 = (un)substituted monocyclic or bicyclic (hetero)aryl; Q = a bond, CO, SO2, or (un)substituted (CH2)0-2CONH, NHCONH, NHCO, or (cyclo)alkylene; R1 = H or (un)substituted alkyl; R2 = a bond or alkylene; or NR1R2V = (un)substituted heterocyclyl; R3-R7 = independently H, halo, NO2, CN, OH, or (un)substituted alkyl, alkoxy, Ph, PhO, carbamoyl, sulfamoyl, acyl, etc.; or R1 and R7 together with the atoms to which they are attached = (un)substituted mono-, di-, or trisubstituted heterocyclyl; V = (un)substituted (hetero)cyclyl or (hetero)aryl; G = a bond or alkylene optionally interrupted by (un)substituted NHSO2NH, CHOH, O, CONH, SO2, NHCONH, NHCO, CO, S, SO2NH, NHSO2, NH, OCO, or NHCO2; M = H or (un)substituted (amino)alkyl, carbamoyl, (hetero)aryl, or (hetero)cycloalkyl; and stereoisomers, mixts., and physiol. tolerable salts thereof] where prepared as reversible inhibitors of the blood clotting enzymes factor Xa (FXa) and/or factor VIIa (FVIIa) with strong antithrombotic effect. For example, 1-[[5-(5-chlorothiophen-2-yl)isoxazol-3-yl]methyl]-1H-indole-2-carboxylic acid was amidated with 1-isopropylpiperidin-4-ylamine•HCl (prepns. given) in the presence of BOP-Cl, Et3N, and DCM and the product purified by preparative HPLC using a H2O/MeCN gradient with 0.1% TFA to afford II•TFA. In a chromogenic assay, the latter exhibited a Ki value of 0.0033 μM against human factor Xa. Thus, I and their pharmaceutical compns. are useful for the therapy and prophylaxis of cardiovascular disorders, such as thromboembolic diseases or restenoses (no data).

IT 681289-24-7P, 1-[[5-(5-Chlorothien-2-yl)isoxazol-3-yl]methyl]-1H-indole-2-carboxylic acid N-[1-(2-dimethylaminoacetyl)piperidin-4-yl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(factor Xa inhibitor; preparation of indolecarboxamides as factor Xa inhibitors for treatment of thrombotic and cardiovascular disorders)

RN 681289-24-7 CAPLUS

CN 1H-Indole-2-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-[2-(dimethylamino)acetyl]-4-piperidinyl]- (CA INDEX NAME)



L6 ANSWER 19 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB Novel β-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRa1 [Ra1 = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ra1 may form a ring], CO, CO2, O2C, CONRa1, S(O)p (p = 0-2), etc.; Ya is absent or O, NRa1, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRa1)r1O(CRaRa1)r-Q (r, r1 = 0-4), (CRaRa1)r1NRa(CRaRa1)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRa1)r1O(CRaRa1)r-Q1, (CRaRa1)r1NRa(CRaRa1)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepared as metalloprotease and TNF-α inhibitors. Thus, N-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepared by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

IT 1055742-94-3

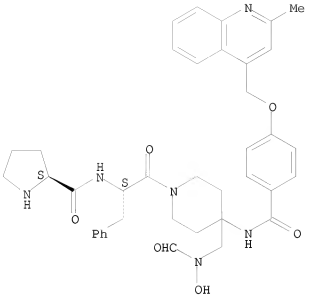
RL: PRPH (Prophetic)

(Preparation of β-amino acid derivatives as inhibitors of matrix metalloproteases and TNF-α)

RN 1055742-94-3 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L6 ANSWER 20 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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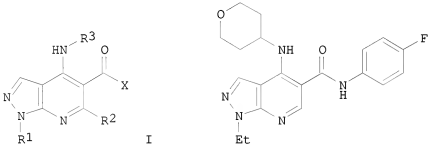
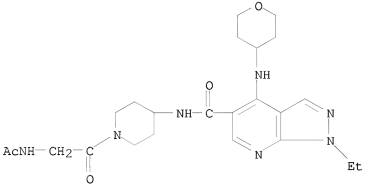


AB Title compds. I [wherein R1 = (fluoro)alkyl, (CH2)2OH, (CH2)2CO2-alkyl; R2 = HMe, fluoroalkyl; R3 = (un)substituted cycloalkyl, cycloalkenyl, or heterocyclyl; X = NR4R5, OR5a; R4 = H, (fluoro)alkyl, (un)substituted cycloalkyl(alkyl); R5 = substituted alkyl, acyl(alkyl), carboxy(alkyl), carbamoyl(alkyl), sulfamoyl(alkyl), alkylsulfonyl(alkyl), or cyano(alkyl); R5a = (fluoro)alkyl, cycloalkyl(alkyl), substituted Ph; and salts thereof] were prepared as phosphodiesterase (PDE) inhibitors, in particular PDE4 inhibitors. The invention also provides for the use of I or pharmaceutically acceptable salts thereof for the treatment and/or prophylaxis of an inflammatory and/or allergic disease, such as chronic obstructive pulmonary disease (COPD), asthma, or allergic rhinitis. For example, 4-chloro-1-ethyl-N-(4-fluorophenyl)1H-pyrazolo[3,4-b]pyridine-5-carboxamide (preparation given) was coupled with 4-aminotetrahydropyran in EtOH using TEA to give II. The latter inhibited human recombinant PDE 4B with a pIC50 of 7.9 and suppressed LPS-induced pulmonary neutrophilia in rats with an ED50 in the range of about 0.5 mg/kg to about 2 mg/kg. In the rat pica model of emesis, II exhibited pica response values (ED50 ranging from 4.8 mg/kg to 40 mg/kg) higher than the neutrophilia-inhibition doses and displayed a therapeutic index >2. Thus, II showed anti-inflammatory effects with low emetic side effects.

IT 675115-92-1P, N-[1-(N-Acetylglycyl)-4-piperidinyl]-1-ethyl-4-[(tetrahydro-2H-pyran-4-yl)amino]-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4 inhibitor; preparation of pyrazolo[3,4-b]pyridines as PDE4 inhibitors for treatment of inflammatory and/or allergic disease)
RN 675115-92-1 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxamide, N-[1-[2-(acetylamino)acetyl]-4-piperidinyl]-1-ethyl-4-[(tetrahydro-2H-pyran-4-yl)amino]- (CA INDEX NAME)



L6 ANSWER 21 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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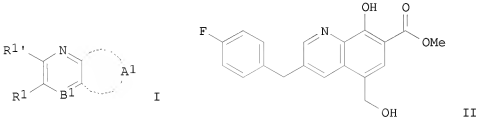
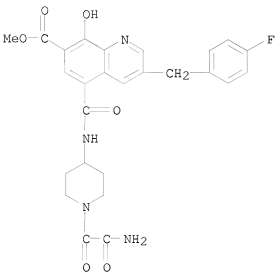


AB The title compds. I [wherein B1 = N or (un)substituted CH; R1 = H, (un)substituted alkyl, alkenyl, etc.; R1' = H, halo, NO2, OH, CO2H, (un)substituted alkoxycarbonyl, alkyl, alkoxy, etc.; A1 = (un)substituted -CH=CH-CH=CH-, -CH=CH-CH=N-, -CH=CH-N=CH-, -CH=CH-O-CH2-, -CH=CH-CH2-O-, or -CH=CH-O-] or prodrugs, solvates, or pharmaceutically acceptable salts thereof are prepared as HIV integrase inhibitors. For example, the compound II was prepared in a multi-step synthesis. II showed inhibitory activity with IC50 of 0.071 μg/mL against integrase. Formulations containing I as an active ingredient were also described.
IT 675611-08-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline and naphthyridine derivs. as HIV integrase inhibitors)
RN 675611-08-2 CAPLUS

CN 7-Quinolinecarboxylic acid, 5-[[[1-(2-amino-2-oxoacetyl)-4-piperidinyl]amino]carbonyl]-3-[(4-fluorophenyl)methyl]-8-hydroxy-, methyl ester (CA INDEX NAME)



L6 ANSWER 22 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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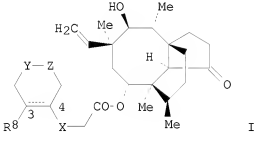


I

AB Pleuromutilin derivs, such as I [X = S, NR; Y = CH2, Z = NR7 or Y = NR7, Z = CH2; R = alkyl; R7 = N-protecting group, such as CO2CMe3, or amino acid derived acyl group such as valyl, histidinyl; R8 = H, OH, acyloxy; 3,4-single or double bond], were prepared for use in pharmaceutical compns. as antimicrobial agents. Thus, 14-O-[N-(tert-butoxycarbonyl)-4-hydroxypiperidin-3-ylsulfanylacetyl]mutilin I (X = S, Y = CH2, Z = NCO2CMe3, R8 = OH, 3,4-single bond), along with its N-(tert-butoxycarbonyl)-3-hydroxypiperidin-4-yl isomer, was prepared via a reaction of thiapleuromutilin with 1-tert-butoxycarbonyl-3,4-epoxypiperidine using Al2O3 in THF. Dosage ranges and drug delivery forms were discussed.

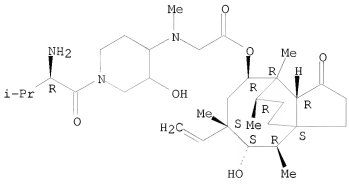
IT 652974-28-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pleuromutilin derivs. for therapeutic use as antimicrobial agents)

RN 652974-28-2 CAPLUS

CN Glycine, N-[1-[(2R)-2-amino-3-methyl-1-oxobutyl]-3-hydroxy-4-piperidinyl]-N-methyl-, (3aS,4R,5S,6S,8R,9R,9aR,10R)-6-ethenyldecahydro-5-hydroxy-

4,6,9,10-tetramethyl-1-oxo-3a,9-propano-3aH-cyclopentacycloocten-8-yl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L6 ANSWER 23 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

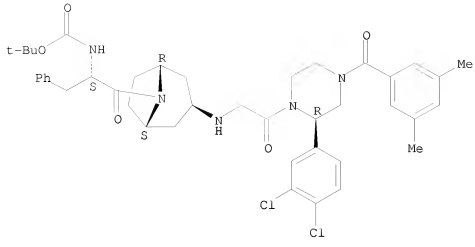
AB The invention discloses a method for treating depression or anxiety in a mammal, including a human, by administering to the mammal a CNS-penetrant NK1 receptor antagonist (e. g., a substance P receptor antagonist) in combination with an NK3 antagonist agent. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a CNS-penetrant NK1 receptor antagonist and an NK3 antagonist.

IT 207405-42-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK1 and NK3 antagonist combination treatment for depression and anxiety)

RN 207405-42-3 CAPLUS

CN Carbamic acid, [(1S)-2-[(3-exo)-3-[[2-[(2R)-2-(3,4-dichlorophenyl)-4-(3,5-dimethylbenzoyl)-1-piperazinyl]-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 24 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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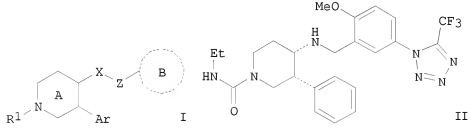


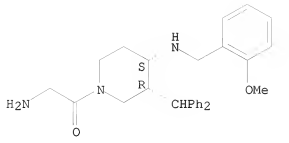
AB The title compds. I [wherein Ar = (un)substituted aryl, aralkyl, or heteroaryl; R1 = H, acyl, (un)substituted hydrocarbyl, or heterocyclyl; X = O or (un)substituted NH; Z = (un)substituted CH2; ring A = (un)substituted piperidine; ring B = (un)substituted aryl; with exclusions] or prodrugs or salts thereof are prepared I have excellent tachykinin receptor antagonistic activity, and are useful for the treatment of frequent urination and urinary incontinence (no data). For example, the compound II•xHCl was prepared in a multi-step synthesis. II showed antagonistic activity with IC50 of 0.025 nM against human substance P receptor. Formulations containing I as an active ingredient were also described.

IT 632346-84-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperidine derivs. as tachykinin receptor antagonists for treatment of frequent urination and urinary incontinence)

RN 632346-84-0 CAPLUS

CN Ethanone, 2-amino-1-[(3R,4S)-3-(diphenylmethyl)-4-[[(2-methoxyphenyl)methyl]amino]-1-piperidinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 25 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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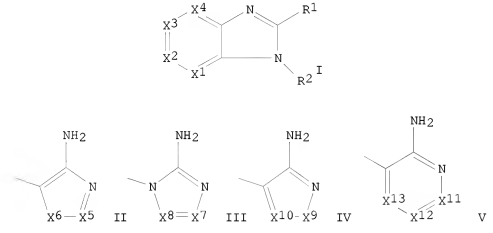


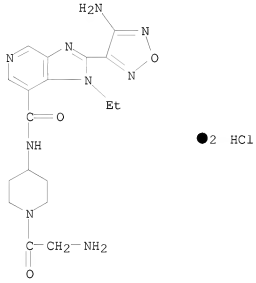
AB This patent concerns imidazopyridines (shown as I; variables defined below; e.g. 4-(1-ethyl-1H-imidazo[4,5-c]pyridin-2-yl)furazan-3-ylamine) and physiol. acceptable salts and or N-oxides thereof, processes for their preparation, pharmaceutical compns. containing them and their use in medicine. For I, X1 is N or CR3; X2 is N or CR4; X3 is N or CR5; X4 is N or CR6 with the proviso that at least one but not more than two of X1, X2, X3 and X4 = N; R1 is a 5-, or 6-membered heterocyclic group II, III, IV or V wherein X5 is a N or CR7: and X6 is a O, S or NR8; X7 and X8, which may be the same or different is a N or CR9; X9 is a O, S or NR8 and X10 is N or CR10; X11, X12 and X13 may be the same or different and = N or R11; addnl. details are given in the claims. For Rho-kinase (ROCK) activity the compds. I of the examples have a pIC50 of 9 to 5.2; for mitogen and stress activated protein kinase-1 (Msk-1) activity the compds. I of the examples have a pIC50 value of 9.28-5.15. The compds. I are essentially non-toxic at therapeutically useful doses; thus no adverse effects were observed when compds. of the invention were administered to rats at a dose of 100 mg/kg. Although no specific therapeutic applications are claimed, because of the inhibition by I of Msk-1, I should be useful for the treatment or prophylaxis of disorders associated with neuronal degeneration resulting from ischemic events or inflammatory conditions, e.g. cerebral stroke; also, because of the inhibition by I of Rho kinases, I should be useful for the treatment or prophylaxis of cardiovascular and neuroinflammatory diseases.

More than 300 example prepns. and/or characterization data for I are included. For example, [4-(1-ethyl-1H-imidazo[4,5-c]pyridin-2-yl)furazan-3-yl]amine was prepared in 4 steps (88, 94, 37 and 43 % yields, resp.) starting from 4-methoxy-3-nitropyridine hydrochloride and ethylamine and involving intermediates ethyl(3-nitropyridin-4-yl)amine, N'-ethylpyridine-3,4-diamine and (1-ethyl-1H-imidazo[4,5-c]pyridin-2-yl)acetonitrile.

IT 607373-50-2P, 2-(4-Aminofurazan-3-yl)-1-ethyl-1H-imidazo[4,5-c]pyridine-7-carboxylic acid N-[1-(2-aminoethanoyl)piperidin-4-yl]amide dihydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of imidazopyridines as kinase inhibitors)

RN 607373-50-2 CAPLUS

CN 1H-Imidazo[4,5-c]pyridine-7-carboxamide, N-[1-(2-aminoacetyl)-4-piperidinyl]-2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-, hydrochloride (1:2) (CA INDEX NAME)



L6 ANSWER 26 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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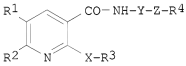


I

AB The invention relates to nicotinamides (shown as I; variables defined below; e.g. anti-2-(benzo[1,3]dioxol-5-yloxy)-N-[4-(2-hydroxybenzoylamino)cyclohexyl]nicotinamide) and to processes for the preparation of, intermediates used in the preparation of, compns. containing and the uses of, such derivs. The nicotinamide derivs. according to the present invention are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic,

respiratory diseases, disorders and conditions, as well as wounds. For I: R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-, -S- or -NH-; R3 = Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl or the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = 4-HNcyclohexyl, piperidin-1,4-diyl, 8-azabicyclo[3.2.1]octane-3,8-diyl, and 4-R5Ncyclohexyl wherein in each the N is bonded to Z in I and R5 = (C1-C4)alkyl and phenyl(C1-C4)alkyl. Z = C(O), C(O)NH, SO2, SO2NH, C(O)CH2NHSO2, SO2NHC(O), C(O)CH2NHC(O) wherein the left end is bonded to Y and the other end to R4; or alternatively Y-Z together = 4-NHC(O)cyclohexyl; R4 = Ph, naphthyl heteroaryl and (C3-C8)cycloalkyl, (un)substituted (C1-C6)alkyl; addnl. details including provisos are given in the claims. The antiinflammatory properties of 72 examples of I are demonstrated by their ability to inhibit TNFα release from human peripheral blood mononuclear cells, e.g. IC50 = 0.014 nM for syn-2-(3,4-difluorophenoxy)-5-fluoro-N-[4-(2-hydroxy-5-methylbenzoylamino)cyclohexyl]nicotinamide. About 200 example prepns. of I and 75 of intermediates are included. For example, to prepare anti-2-[(benzo[1,3]dioxol-5-yl)oxy]-N-[4-[(2-hydroxybenzoyl)amino]cyclohexyl]nicotinamide (160.7 mg), 2-hydroxybenzoic acid (0.767 mmol), 1-hydroxybenzotriazole hydrate (1.15 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.15 mmol) were stirred in DMF (5 mL) under an atmospheric of N2 at room temperature for 1.5 h.

Anti-N-(4-aminocyclohexyl)-2-[(benzo[1,3]dioxol-5-yl)oxy]nicotinamide hydrochloride (0.767 mmol; preparation given) and N-methylmorpholine (0.767 mmol) were then added, and the reaction mixture stirred at room temperature for a

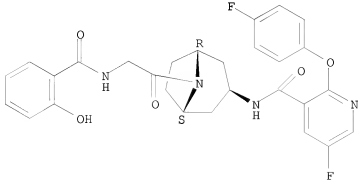
further 18 h.

IT 582331-47-3P, 5-Fluoro-2-(4-fluorophenoxy)-N-[exo-8-[[(2-hydroxybenzoyl)amino]acetyl]-8-azabicyclo[3.2.1]oct-3-yl]nicotinamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of nicotinamides useful as PDE4 inhibitors for treating diseases including inflammatory, allergic and respiratory diseases)

RN 582331-47-3 CAPLUS

CN 3-Pyridinecarboxamide, 5-fluoro-2-(4-fluorophenoxy)-N-[(3-exo)-8-[2-[(2-hydroxybenzoyl)amino]acetyl]-8-azabicyclo[3.2.1]oct-3-yl]- (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 27 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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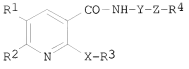


I

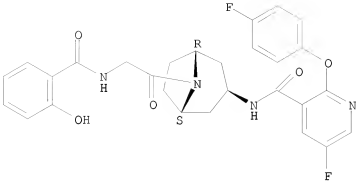
AB The invention relates to a combination of nicotinamides (shown as I; variables defined below; e.g. anti-2-(benzo[1,3]dioxol-5-yloxy)-N-[4-(2-hydroxybenzoylamino)cyclohexyl]nicotinamide) and tiotropium or a derivative thereof, compns. containing them and the uses of, such combinations. The nicotinamide derivs. according to the present invention are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic, respiratory diseases, disorders and conditions, as well as wounds. For I: R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-, -S- or -NH-; R3 = Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl or the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = 4-HNcyclohexyl, piperidin-1,4-diyl, 8-azabicyclo[3.2.1]octane-3,8-diyl, and 4-R5Ncyclohexyl wherein in each the N is bonded to Z in I and R5 = (C1-C4)alkyl and phenyl(C1-C4)alkyl. Z = C(O), C(O)NH, SO2, SO2NH, C(O)CH2NHSO2, SO2NHC(O), C(O)CH2NHC(O) wherein the left end is bonded to Y and the other end to R4; or alternatively Y-Z together = 4-NHC(O)cyclohexyl; R4 = Ph, naphthyl heteroaryl and (C3-C8)cycloalkyl, (un)substituted (C1-C6)alkyl; addnl. details including provisos are given in the claims. The antiinflammatory properties of 72 examples of I are demonstrated by their ability to inhibit TNFα release from human peripheral blood mononuclear cells, e.g. IC50 = 0.014 nM for syn-2-(3,4-difluorophenoxy)-5-fluoro-N-[4-(2-hydroxy-5-methylbenzoylamino)cyclohexyl]nicotinamide. About 200 example prepns. of I and 75 of intermediates, the same as in WO 03/068235 A1, are included.

IT 582331-47-3P, 5-Fluoro-2-(4-fluorophenoxy)-N-[exo-8-[[(2-hydroxybenzoyl)amino]acetyl]-8-azabicyclo[3.2.1]oct-3-yl]nicotinamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; nicotinamide PDE4 inhibitors in combination with tiotropium muscarinic receptor antagonists for treating inflammatory, allergic and respiratory diseases)

RN 582331-47-3 CAPLUS

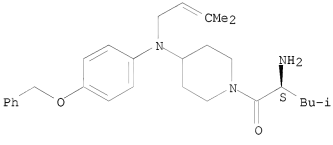
CN 3-Pyridinecarboxamide, 5-fluoro-2-(4-fluorophenoxy)-N-[(3-exo)-8-[2-[(2-hydroxybenzoyl)amino]acetyl]-8-azabicyclo[3.2.1]oct-3-yl]- (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 28 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Disclosed are medicinal compns. useful as preventives/remedies for pain which comprise gabapentin, pregabalin or pharmaceutically acceptable salts thereof combined with N-type calcium channel antagonists or pharmaceutically acceptable salts thereof having specified structures. A compound N-[3-[4-(5H-dibenzo[a,d][7]annulene-5-ylidene)-1-piperidinyl]-3-oxopropyl]-2,2-dimethylpropanamide (I) was prepared The analgesic effect of oral administration of gabapentin 100 mg/kg combined with the compound I 3 mg/kg in pain rat model was examined
IT 250237-01-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicinal compns. containing gabapentin or pregabalin and N-type calcium channel antagonist)
RN 250237-01-5 CAPLUS
CN 1-Pentanone, 2-amino-4-methyl-1-[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 29 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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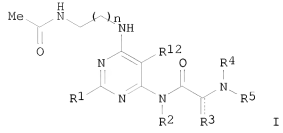

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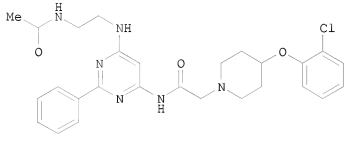


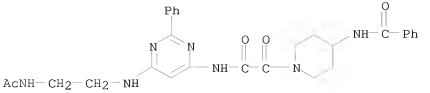
II

AB Title compds. I [wherein R1 = (un)substituted Ph, heterocyclyl, or heteroaryl; R2 and R3 = independently H or (un)substituted (cyclo)alkyl, alkanoyl, alkoxy(carbonyl), alkenyl, monocyclic or bicyclic aryl, heteroaryl, or heterocyclyl; or R2 and R3 are joined to form a heterocyclic ring; wherein the dashed line = a double bond which may be present or absent, and when present R3 = O; R4 and R5 = independently (un)substituted (cyclo)alkyl, alkanoyl, alkoxy(carbonyl), alkenyl, monocyclic or bicyclic aryl, heteroaryl, or heterocyclyl; or NR4R5 = (un)substituted monocyclic or bicyclyl, heterocyclyl, or heteroaryl; R12 = H, alkyl, halo, or cyano; n = 0-4; or enantiomers, tautomers, or pharmaceutically acceptable salts thereof] were prepared as A2b adenosine receptor antagonists. For example, cycloaddn. of benzamidine•HCl and di-Et malonate using DBU in DMF gave 2-phenylpyrimidine-4,6-diol (73%). Chlorination (95%), amination (93%), substitution with N-(2-aminoethyl)acetamide (57%), and amidation with chloroacetyl chloride (91%) provided N-[6-(2-acetylaminoethylamino)-2-phenylpyrimidin-4-yl]-2-chloroacetamide. Coupling of the chloroacetamide with 4-(2-chlorophenoxy)piperidine in the presence of NaI and DIPEA in 3:1 acetonitrile:THF afforded II (86%). Compds. of the invention showed greater than tenfold selectivity for the human A2b adenosine receptor (Ki values <100 nM) over the A1, A2a, and A3 receptors in radioligand binding assays. Thus, I and pharmaceutical comps. comprising I are useful for the treatment of diseases associated with the A2b adenosine receptor, such as asthma, diabetes, or proliferating tumors associated with mast cell degranulation (no data).

IT 552870-71-0P, N-[1-[2-[[6-[[2-(Acetylamino)ethyl]amino]-2-phenylpyrimidin-4-yl]amino]-2-oxoacetyl]piperidin-4-yl]benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A2b antagonist; preparation of N-(pyrimidinyl)acetamides as A2b adenosine receptor selective antagonists for treatment of asthma, diabetes, tumors, and other A2b associated diseases)

RN 552870-71-0 CAPLUS

CN 1-Piperidineacetamide, N-[6-[[2-(acetylamino)ethyl]amino]-2-phenyl-4-pyrimidinyl]-4-(benzoylamino)-α-oxo- (CA INDEX NAME)



L6 ANSWER 30 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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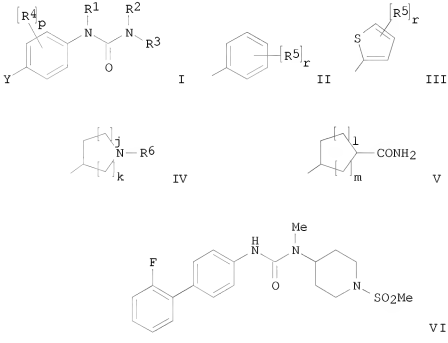


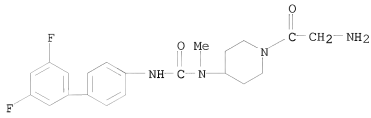
AB The title compds. [I; Y = II, III; R1 = H, alkyl; R2 = H, alkyl, cycloalkyl, etc.; R3 = IV, V, etc.; j = 0-2; k = 1-2; l = 0-2; m = 0-2; p = 1-3; r = 1-3; R4 = H, OH, halo, etc.; R5 = H, halo, OH, etc.; R6 = alkylSO2, cycloalkylSO2, heteroarylalkyl, etc.;], useful as neuropeptide Y5 receptor antagonists for treating obesity, hyperphagia, type II diabetes, insulin resistance, and hypertension, were prepared E.g., a multi-step synthesis of VI, was given. For the compds. I, a range of neuropeptide Y5 receptor binding activity from about 0.2 nM to about 500 nM was observed Methods of preparing pharmaceutical formulations comprising one
or more such compds. I were claimed.

IT 405055-71-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted ureas as neuropeptide Y5 receptor antagonists)

RN 405055-71-2 CAPLUS

CN Urea, N-[1-(2-aminoacetyl)-4-piperidinyl]-N'-(3',5'-difluoro[1,1'-

biphenyl]-4-yl)-N-methyl- (CA INDEX NAME)



L6 ANSWER 31 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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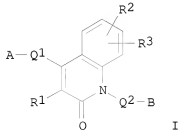


I

AB Title derivs. I [Q1 = bond, CH2, CH2CH2, vinyl, CHMe, etc.; A = lower alkyl, (un)substituted cycloalkyl (condensed with hydrocarbyl ring), (un)substituted aryl, (un)substituted heterocyclyl (condensed with hydrocarbyl ring); R1 = H, lower alkyl; R2, R3 = H, (un)substituted lower alkyl(oxy), aralkyloxy, piperidinyl, etc.; R2R3 may be linked to form lower alkylenedioxy; Q2 = bond, CH2, CH2CH2, etc.; B = CO2H, lower alkoxycarbonyl, (un)substituted 2-pyridinyl, (un)substituted Ph, (un)substituted cyclohexyl, etc.] or their salts are claimed. The derivs. are also useful for termination of delivery prior to Caesarean section. Thus, 4-(2,3-dimethoxyphenyl)-7-methoxy-2-oxoquinoline was treated with Me 4-bromomethylbenzoate to give 56% I (AQ1 = 2,3-dimethoxyphenyl, R1-R3 = H, Q2B = 4-CH2C6H4CO2Me), which inhibited binding of [3H]-oxytocin to its receptor with IC50 of 0.972 μmol/L.

IT 528831-20-1P

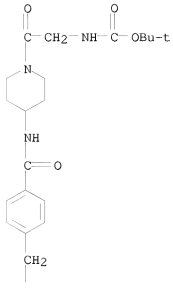
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of carbostyryl derivs. as oxytocin antagonists)

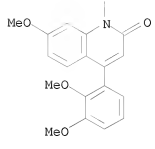
RN 528831-20-1 CAPLUS

CN Carbamic acid, [2-[4-[[4-[[4-(2,3-dimethoxyphenyl)-7-methoxy-2-oxo-1(2H)-quinolinyl]methyl]benzoyl]amino]-1-piperidinyl]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L6 ANSWER 32 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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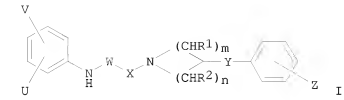
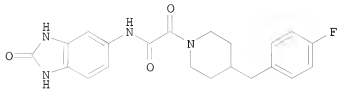


I



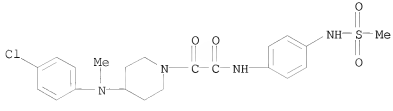
II

AB The title compds. I [wherein V and U = independently H, halo, OH, CN, NO2, NH2, alkylsulfonyloxy, carboxyl, CF3, CF3O, alkyl-SO2-NHCH2, NH2-(CH2)1-4-SO2NH, NH2-(CH2)1-4-CONH, sulfamoyl, CHO, aminomethyl, HOCH2, alkyl, alkoxymethyl, halo-CH2, tetrazolyl, alkoxy(carbonyl), alkanoyloxy, Ph, (un)substituted alkylamino, arylamino, aralkylamino, alkylsulfonamido, alkanoylamido, arylsulfonamido, or alkoxy groups; or the neighboring V and U together form (un)substituted 4-7 membered ring with the atoms attached; W and X = independently CO, CH2, or CH-alkyl; Y = O, (cyclo)alkylene, alkynylene, aminocarbonyl, NH, N-alkyl, CH2O, CH(OH), or OCH2; Z = H, halo, NO2, NH2, alkyl, alkoxy, CN, CF3, OH, or CO2H; R1 and R2 = independently H or alkyl; or R1 and R2 together form (un)substituted C1-C3 bridge; n and m = independently 0-3 with restriction that n and m ≠ 0 at the same time; with provisos] and optical antipodes, racemates, or pharmaceutically acceptable salts thereof are prepared as NMDA receptor antagonists, and moreover most of the compds. are selective antagonist of NR2B subtype of NMDA receptor. For example, 2-[4-(4-fluorobenzyl)piperidin-1-yl]-2-oxoacetic acid (prepn given) was treated with 5-amino-1,3-dihydroindol-2-one in DMF in the presence of Et3N and HBTU to afford the acetamide II (48%). II showed IC50 of 0.0007 μM against NMDA in rat. Formulations containing I as an active ingredient were also described.

IT 496058-31-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NMDA receptor antagonist; preparation of piperidinylacetamides by coupling reactions as NMDA receptor antagonists)

RN 496058-31-2 CAPLUS

CN 1-Piperidineacetamide, 4-[(4-chlorophenyl)methylamino]-N-[4-[(methylsulfonyl)amino]phenyl]-α-oxo- (CA INDEX NAME)



L6 ANSWER 33 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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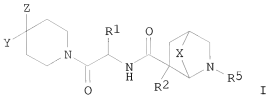


I

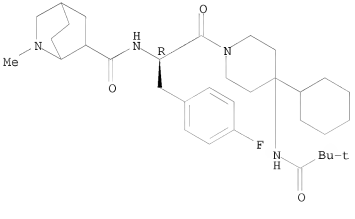
AB Novel bridged piperidine derivs. I [R1 = H or (un)substituted alkyl, (CHR7)0-2cycloalkyl, (CHR7)1-2O(CHR7)aryl, or (CHR7)0-2-(hetero)aryl, where R7 = H or (un)substituted alkyl, (CH2)0-2phenyl, -naphthyl, -heteroalkyl, or -cycloalkyl; or two R7 groups may form a ring; R2 = H, alkyl, (CH2)0-2cycloalkyl or -aryl; X = (CR3R4)1-2, where R3, R4 = H, alkyl, (CH2)0-2cycloalkyl or -aryl, OH, halo, or amino; R5 = H, alkyl, (CH2)0-2-(hetero)aryl, -cycloalkyl, or -heterocyclyl, acyl, CH2C.tplbond.CH, CO2R7, CH2CHF2, CONR72, SO2R7, etc.; Y = H, (un)substituted alk(en)yl, (CH2)0-2cycloalkyl, -Ph,-naphthyl, -heteroaryl, or -heterocyclyl; Z = alkyl or (CH2)0-2 attached to certain rings or functional groups] were prepared as agonists of human melanocortin receptor(s), in particular, the human melanocortin-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, and sexual dysfunction. Thus, I (R1 = p-FC6H4CH2, R2 = R5 = H, X = CH2, Y = cyclohexyl, Z = Me3CNHCO) was prepared as diastereomers via a coupling reaction. Compds. of the invention were found to bind to MC-4R (IC50 < 2 μM, EC50 < 1 μM).

IT 491853-44-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bridged piperidine amino acid derivs. as melanocortin receptor agonists)

RN 491853-44-2 CAPLUS

CN 2-Azabicyclo[2.2.2]octane-6-carboxamide, N-[(1R)-2-[4-cyclohexyl-4-[(2,2-dimethyl-1-oxopropyl)amino]-1-piperidinyl]-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 34 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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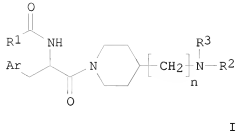
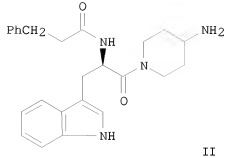
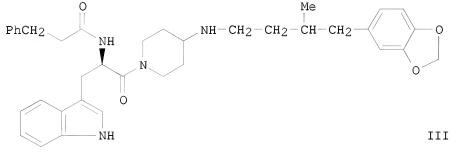


I



II



III

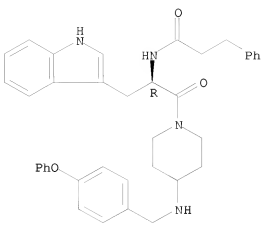
AB Title compds. I [R1 = (un)substituted alkylphenyl, heteroaryl, alkyl, etc.; R2 = (un)substituted alkylnaphthyl, alkylphenyl, alkylfluorenyl, etc.; R4 = H, (un)substituted alkylnaphthyl, alkylfluorenyl, etc.; Ar = (un)substituted Ph, naphthyl, indolyl] were prepared For example, reductive amination of amine II, e.g., prepared from D-tryptophan in 3-steps, and 3-(3,4-methylenedioxyphenyl)-2-methylpropanal afforded claimed carbonylpiperidine III. In stimulation of the human GPR38 motilin receptors, 10 specific examples of compds. showed a stimulation of at least 60 %. Approx. 2-specific examples of compds. I and 5-intermediates were prepared

IT 1099124-32-9
RL: PRPH (Prophetic)
(Preparation of 1-amidomethylcarbonylpiperidines as human motilin receptor (GPR38) agonist for the treatment of gastrointestinal motility disorders)

RN 1099124-32-9 CAPLUS

CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L6 ANSWER 35 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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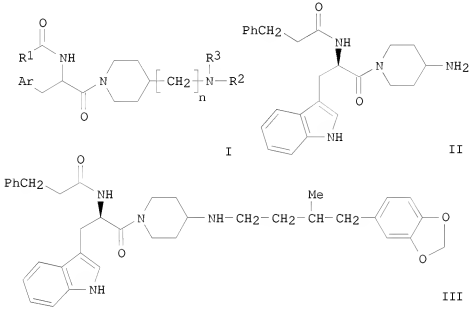


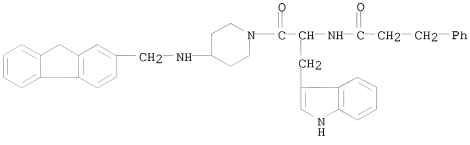
AB Title compds. I [R1 = (un)substituted alkylphenyl; R2 = (un)substituted alkylnaphthyl, alkylfluorenyl, alkylphenyl, etc.; R4 = H, (un)substituted alkylnaphthyl, alkylfluorenyl, etc.; Ar = (un)substituted Ph, naphthyl, indolyl; n = 0-3] were prepared For example, reductive amination of amine II, e.g., prepared from D-tryptophan in 3-steps, and 3-(3,4-methylenedioxyphenyl)-2-methylpropanal afforded claimed carbonylpiperidine III. In stimulation of the human GPR38 motilin receptors, 10 specific examples of compds. showed a stimulation of at least 60 %. Approx. 2-specific examples of compds. I and 5-intermediates were prepared

IT 475634-01-6
RL: PRPH (Prophetic)

(Preparation of 1-amidomethylcarbonylpiperidines as human motilin receptor (GPR38) agonist for the treatment of gastrointestinal motility disorders)

RN 475634-01-6 CAPLUS

CN Benzenepropanamide, N-[2-[4-[(9H-fluoren-2-ylmethyl)amino]-1-piperidinyl]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]- (CA INDEX NAME)



L6 ANSWER 36 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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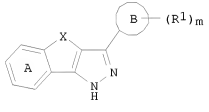
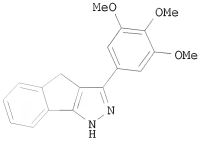


I



II

AB Title compds. I [m = 1-10; X = alkyl, CO, O, oximino, etc.; B = alkyl, cycloalkyl, aryl, pyridyl, thienyl, furyl, pyrrolyl; R1 = H, halo, hydroxy, nitro, cyano, hydroxyamidino, etc.; A = (un)substituted with one or more substituents selected from halo, alkyl, etc.] were prepared For instance, indan-1-one hydrazone (preparation given) was reacted with Me 3,4,5-trimethoxybenzoate (THF, n-BuLi, 0°) and subsequently acidified with HCl (3 M) and heated to reflux for 1 h to give II. I are inhibitors of protein kinase activity and used for the treatment of, e.g., cancer, diabetic retinopathy, etc.

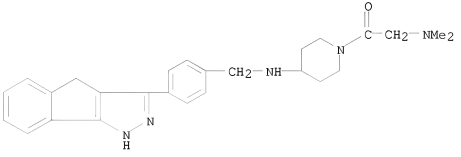
IT 374903-38-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(kinase inhibitor; 3-(hetero)aryl pyrazoles with 4,5(3,4)-bicyclic ring fusion as protein kinase inhibitors)

RN 374903-38-5 CAPLUS

CN Ethanone, 1-[4-[[[4-(1,4-dihydroindeno[1,2-c]pyrazol-3-yl)phenyl]methyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 37 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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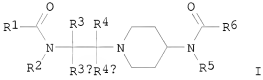


I

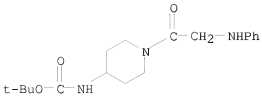
AB The title compds. [I; R1 = (un)substituted cycloalkyl, cycloalkenyl, heterocyclyl, etc.; R2 = Ph, heteroaryl, phenylalkyl, heteroalkyl; R3, R3a, R4, R4a = H, alkyl; R5 = H, alkyl, haloalkyl, etc.; R6 = Ph, heteroaryl, PhNH, etc.], useful as modulators of chemokine activity (especially CCR5 activity), were prepared and formulated. Thus, treating cyclobutanecarboxylic acid with oxalyl chloride in DCM followed by reaction of N-[1-(N-phenyl-2-ethylamino)-4-piperidinyl]-N-methyl-4-fluorophenylacetamide (preparation given) with the resulting acid chloride in the presence of (iso-Pr)2NEt in DCM afforded I [R1 = cyclobutyl; R2 = Ph; R3, R3a, R4, R4a = H; R5 = Me; R6 = CH2Ph-4-F]. Certain compds. I showed IC50 of < 50 μM in RANTES or MIP-1α binding assay.

IT 463934-38-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel N-(2-piperidinoethyl) amides as modulators of chemokine receptors)

RN 463934-38-5 CAPLUS

CN Carbamic acid, [1-[(phenylamino)acetyl]-4-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 38 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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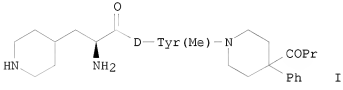


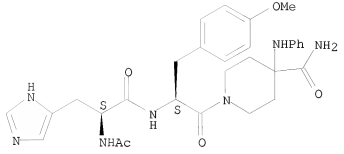
AB Compds. W-(CR6R7)yCH(G)(CR4R5)xCO-X(R1)CHR2(CHR3)r(CH2)sCO-E [X = N or CH; R1, R3 = H or alkyl; R2 = H, aryl, cycloalkyl, heteroaryl, heterocyclyl, (un)substituted alkyl or alkenyl; R1 together with R2 or R3 or R2 together with R3 form mono- or bicyclic aryl, cycloalkyl, heteroaryl, or heterocyclyl; E = (un)substituted pyrrolidino, piperidino, hexahydro-1-azepinyl, 1-piperazinyl, cyclopentyl, cyclohexyl, cycloheptyl, amino, (cyclo)alkylamino; R4-R6 = H, (un)substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclyl; or CR4R5 or C6R7 is a spirocycloalkyl ring; r, s = 0 or 1; x = 0-4; y = 0-2; G = alkenyl, arylalkenyl, hydroxy, heteroaryl, cyano, functionalized alkyl or alkenyl, etc.; W = amino, alkylamino, hydroxy, alkoxy, carbamoyl, amidino, cycloalkyl, heteroaryl, heterocyclyl, etc.] were prepared as modulators of melanocortin receptors, particularly MC-1R and MC-4R. Thus, peptide I was prepared by a solution-phase peptide coupling/deprotection scheme.

IT 457903-95-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for pharmaceutical use as modulators of melanocortin receptors)

RN 457903-95-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[(2S)-2-[[(2S)-2-(acetylamino)-3-(1H-imidazol-5-yl)-1-oxopropyl]amino]-3-(4-methoxyphenyl)-1-oxopropyl]-4-(phenylamino)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 39 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB In order to obtain more potent growth hormone secretagogues, a comparison of ipamorelin and NN703 suggested the addition of a polar group at the C-terminus of NN703. A study was conducted using constrained amines for this purpose. Here, substituted 4-piperidinylamino- and 4-dimethylaminopiperidino-substituents were found to give the most active compds. A replacement of the 4-dimethylaminopiperidino-substituent with 4-hydroxypiperidino resulted in a series of compds., which showed in vitro activity with EC50 values in the low nanomolar range, and favorable kinetic properties, such as 40% oral bioavailability. The most promising compound was also tested in a swine in vivo model, resulting in a growth hormone level with a Cmax of over 40 ng mL-1.

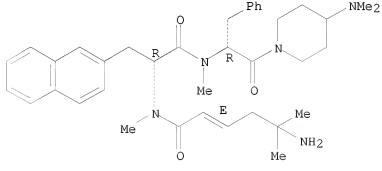
IT 254905-32-3P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(influence of conformational restriction in C-terminus on the potency of growth hormone secretagogues)

RN 254905-32-3 CAPLUS

CN 4-Piperidinamine, 1-[N-[(2E)-5-amino-5-methyl-1-oxo-2-hexen-1-yl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N-methyl-D-phenylalanyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 40 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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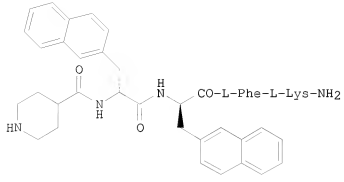


I

AB The present invention comprises growth hormone releasing peptides/peptidomimetics (GHRP) capable of causing release of growth hormone from the pituitary. Compns. containing the GHRPs of this invention are used to promote growth in mammals either alone or in combination with other growth promoting compds., especially insulin-like growth factor-1 (IGF-1).

In a method of this invention, GHRPs in combination with IGF-1 are used to treat type II diabetes. Thus, I.CF3CO2H was prepared by standard solid-phase methods on an aminomethyl resin using 9-fluorenylmethoxycarbonyl (Fmoc) Nα protection. I induced significant body weight and organ weight gain in rats.

IT 179383-00-7P

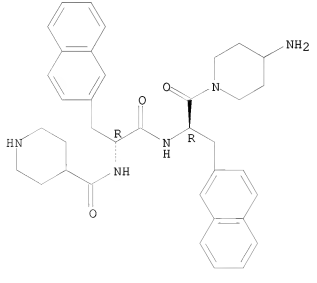
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of low mol. weight peptide mimics as growth hormone release stimulators)

RN 179383-00-7 CAPLUS

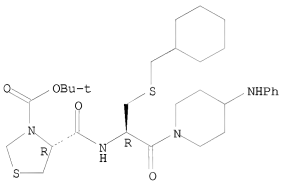
CN 4-Piperidinecarboxamide, N-[(1R)-2-[[(1R)-2-(4-amino-1-piperidinyl)-1-(2-naphthalenylmethyl)-2-oxoethyl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 41 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB This study was performed to determine the structure-activity relationships (SAR) of l-cysteine based N-type calcium channel blockers. Basic nitrogen was introduced into the C-terminal lipophilic moiety of l-cysteine with a view toward improvement of its physicochem. properties. One of L-cysteine derivative was found to be a potent and selective N-type calcium channel blocker with IC50 of 0.33 μM in calcium influx assay using IMR-32 cells and was 15-fold selective for N-type calcium channels over L-type channels. One of the compds. showed improved oral analgesic efficacy in the rat formalin induced pain model and the rat chronic constriction injury (CCI) model, which is one of the most reliable models of chronic neuropathic pain, without any significant effect on blood pressure or neurol. behavior.
IT 253306-59-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-activity relationship and oral analgesic efficacy of L-Cysteine based N-type calcium channel blockers in rat pain models)
RN 253306-59-1 CAPLUS
CN 3-Thiazolidinecarboxylic acid, 4-[[[(1R)-1-[[(cyclohexylmethyl)thio]methyl]-2-oxo-2-[4-(phenylamino)-1-piperidinyl]ethyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (4R)- (9CI) (CA INDEX NAME)

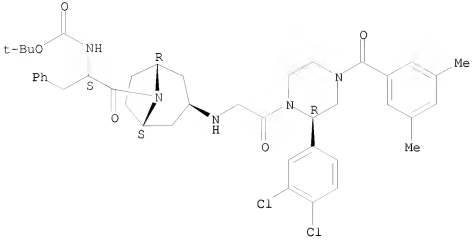
Absolute stereochemistry.



L6 ANSWER 42 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB A composition for the treatment of anxiety or depression in a mammal, including a human, comprises (a) an NK-3 receptor antagonist or its salt, (b) a CNS-penetrant NK-1 receptor antagonist or its salt, and (c) a pharmaceutically acceptable carrier. When administered in combination, either as a single or as sep. pharmaceutical composition(s), the CNS-penetrant NK-1 receptor antagonist and an NK-3 antagonist, are presented in a ratio which is consistent with the manifestation of the desired effect. In particular, the ratio by weight of the CNS-penetrant NK-1 receptor antagonist and the NK-3 antagonist will suitably be between 0.001:1 to 1000:1, and especially between 0.01:1 and 100:1.
IT 207405-42-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of NK3 receptor antagonist and CNS-penetrant NK1 receptor antagonist for treating depression and anxiety)
RN 207405-42-3 CAPLUS
CN Carbamic acid, [(1S)-2-[(3-exo)-3-[[2-[(2R)-2-(3,4-dichlorophenyl)-4-(3,5-dimethylbenzoyl)-1-piperazinyl]-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA

INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 43 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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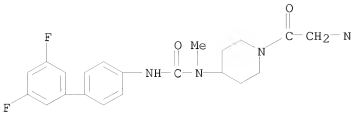
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; A = Q, Q1; R1 = H, F, Cl, CF3, OH; R2 = H, F, Cl, CF3, CN, OCH3, OH; R3 = H, F, Cl, CF3, OCF3, CN, OCH2C6H5, OH; R4 = H, F, Cl; X = NH, NCH3; n = 0, 1, 2; Y = NR5, C:NOH; R5 = SO2CH3, SO2(CH2)2CH3, cyclopropylmethyl, 3-pyridyl, 2-pyridyl, 2-thiazolyl, 2-pyrimidyl, 1-oxo-3-pyridyl, SO2NH2, CH2CONH2, CONH2, NHSO2CH3, SO2(CH2)2OH, C(:NCN)NHCH3, C(:NCN)SCH3, 3-pyridylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, CON(CH3)2, cyclohexyl; R6 = H, F, Br, Cl, OCH3, OH; R7 = H, F, Cl, OCH3; etc.], stereoisomers, N-oxides, pharmaceutically acceptable salts or hydrates, and prodrugs are disclosed as neuropeptide Y5 receptor antagonists. Method of treating obesity, hyperphagia, type II diabetes, insulin resistance, and hypertension involving title compds. I are claimed. Thus, the title compound II was prepared from N-tert-butoxycarbonyl-4-piperidone, 4-bromophenyl isocyanate, 2-fluorophenylboronic acid, and methanesulfonyl chloride in multiple steps.

IT 405055-71-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted ureas as neuropeptide Y5 receptor antagonists)

RN 405055-71-2 CAPLUS

CN Urea, N-[1-(2-aminoacetyl)-4-piperidinyl]-N'-(3',5'-difluoro[1,1'-biphenyl]-4-yl)-N-methyl- (CA INDEX NAME)



L6 ANSWER 44 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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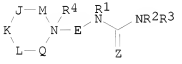


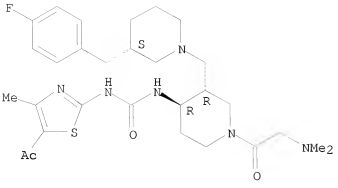
AB Title compds. [I; M = null, CHR5, CHR13, CR13R13, CR5R13; Q = CH2, CHR5, CHR13, CR13R13, CR5R13; J, K = CH2, CHR5, CHR6, CR6R6, CR5R6; L = CHR5, CR5R6; when M = null, J = CH2, CHR5, CHR13, CR5R13; Z = O, S, NR1a, C(CN)2, CH(NO2), CHCN; R1a = H, alkyl, cycloalkyl, CONR1bR1b, OR1b, CN, NO2, (alkyl)phenyl; R1b = H, alkyl, cycloalkyl, Ph; E = G(CHR')mB(CHR')m; G = bond, CO, SO2; B = (substituted) 5-7 membered saturated heterocyclyl; R1, R2 = H, alkyl, alkenyl, alkynyl, (alkyl)cycloalkyl; R3 = (substituted) alkyl, alkenyl, alkynyl, fluoroalkyl, haloalkyl, (alkyl)carbocyclyl, (alkyl)heterocyclyl; R4 = null, O, alkyl, alkenyl, alkynyl, etc.; R5 = (substituted) (alkyl)cycloalkyl, alkylheterocyclyl; R6 = alkyl, alkenyl, alkynyl, (alkyl)cycloalkyl, etc.; R13 = alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R' = H, alkyl, alkenyl, alkynyl, etc.; m = 0-2], were prepared as modulators of CCR3 chemokine receptor activity (no data). Thus, (3R,4R)-4-amino-3-[(S)-3-(4-fluorobenzyl)piperidine-1-carbonyl]piperidine-1-carboxylic acid tert-Bu ester (preparation given) in THF/Et3N was treated with 3-acetylphenyl isocyanate followed by stirring for 17 h to give 62% (3R,4R)-4-[3-(3-acetylphenyl)ureido]-3-[(S)-3-(4-fluorobenzyl)piperidine-1-carbonyl]piperidine-1-carboxylic acid tert-Bu ester. [This abstract record is one of 20 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

IT 388099-60-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-ureidoheterocyclylalkylpiperidines as modulators of CCR3 chemokine receptor activity)

RN 388099-60-3 CAPLUS

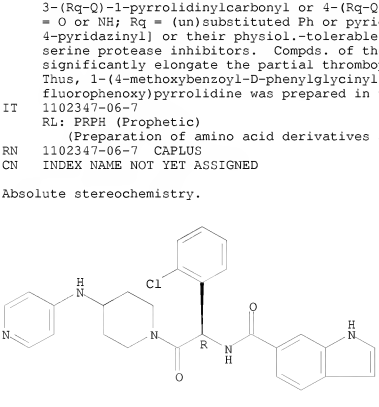
CN Urea, N-(5-acetyl-4-methyl-2-thiazolyl)-N'-[(3R,4R)-1-[2-(dimethylamino)acetyl]-3-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]-4-piperidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 45 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 is a 5- or 6-membered aromatic carbon ring optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5- or 6-membered carbocyclic or heterocyclic ring, or substituted at the position alpha to X-X; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)saturated, mono- or polycyclic, homo- or heterocyclic group; -L-Lp(D)n is 3-(Rq-Q)-1-pyrrolidinylcarbonyl or 4-(Rq-Q)-1-piperidinylcarbonyl, where Q = O or NH; Rq = (un)substituted Ph or pyridyl, 4-pyrimidinyl, 3- or 4-pyridazinyl] or their physiol.-tolerable salts were prepared for use as serine protease inhibitors. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 1-(4-methoxybenzoyl-D-phenylglycinyl)-3-(R,S)(2-fluorophenoxy)pyrrolidine was prepared in the first of 54 examples.
IT 1102347-06-7
RL: PRPH (Prophetic)
(Preparation of amino acid derivatives as serine protease inhibitors)
RN 1102347-06-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L6 ANSWER 46 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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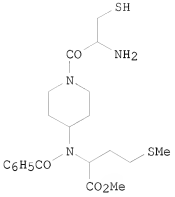


I

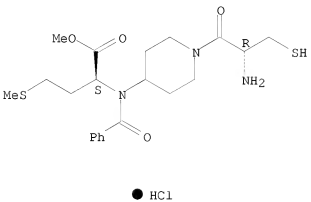
AB New CA1A2X peptidomimetics are described as Ras farnesyl transferase inhibitors (FTIs). They include cysteine and methionine as mimetics of the C-terminus sequence of farnesylated proteins. Furthermore, cysteine was replaced by heterocycles, taking into account the role of zinc and the metabolic instability of amino acids. The mol. docking of (I) in the active site of the enzyme and the pharmacol. evaluation of the compds. are illustrative of a new class of FTIs.

IT 227314-71-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis, and pharmacol. evaluation of new farnesyl protein transferase inhibitors)

RN 227314-71-8 CAPLUS

CN L-Methionine, N-[1-[(2R)-2-amino-3-mercapto-1-oxopropyl]-4-piperidinyl]-N-benzoyl-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 47 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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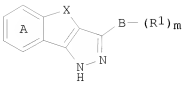


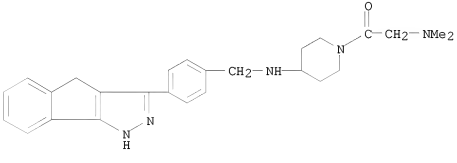
I

AB Title compds. I [m = 1-10; X = (CH2)n, CO, O, C:NOR10, NR11, (CH2)n, S, SO, or SO2; n = 1-3; R10 = alkyl; R11 = (un)substituted alkyl or Ph; B = (cyclo)alkyl, aryl, pyridyl, thienyl, furyl, or pyrrolyl; R1 = H, halo, OH, NO2, CN, hydroxyamidino, CH2NH2, formamidomethyl, (un)substituted alkenyl(oxy), alkynyl, or YW; Y = absent or alkyl, alkoxy, O, S, or CO; W = H, OH, (un)substituted Ph, alkoxy, or amino; ring A is optionally substituted with halo, OH, NO2, CN, or (un)substituted alkyl, alkoxy, PhO, carboxy, carbamoyl, amino, amido, aralkyl, alkenyl, or alkynyl; with provisos; and racemic mixts., racemic diastereomeric mixts., tautomers, optical isomers, and pharmaceutically acceptable salts thereof] were prepared as protein kinase inhibitors, especially tyrosine kinase inhibitors. Thus, indan-1-one hydrazone (preparation given) in THF at 0° was treated with BuLi and then with Me 3,4,5-trimethoxybenzoate to give 3-(3,4,5-trimethoxyphenyl)-1,4-dihydroindeno[1,2-c]pyrazole. Example compds. significantly inhibited KDR kinase at concns. of ≤ 50 μM.

IT 374903-38-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic pyrazole derivs. as tyrosine kinase inhibitors for treatment of angiogenesis-related diseases)

RN 374903-38-5 CAPLUS

CN Ethanone, 1-[4-[[[4-(1,4-dihydroindeno[1,2-c]pyrazol-3-yl)phenyl]methyl]amino]-1-piperidinyl]-2-(dimethylamino)- (CA INDEX NAME)



L6 ANSWER 48 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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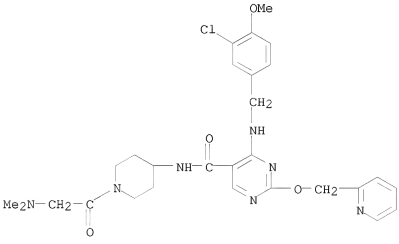
I

AB Compds. of the general formula (I) or pharmacol. acceptable salts thereof [wherein X is :CH or N; Y is NH, NR4, S, O, CH:N, N:CH, N:N, CH:CH, or the like; R1 is lower alkoxy, amino, a nitrogenous heterocyclic group, or a hydroxyl group substituted with a heterocyclic group (wherein each group may be substituted); R2 is either a lower alkylamino or lower alkoxy group which may be substituted with aryl, or a lower alkoxy group substituted with a nitrogenous aromatic heterocyclic group; and R3 is aryl, a nitrogenous heterocyclic group, lower alkyl, lower alkoxy, lower cycloalkoxy, a hydroxyl group substituted with a nitrogenous heterocyclic group, or amino (wherein each group may be substituted), or alternatively, R3 and the substituent of Y may be united to form a lactone ring] or pharmacol. acceptable salts thereof are prepared These compds. exhibit excellent PDE V inhibitory activity and are useful as preventive or therapeutic agents for various diseases due to dysfunction of the signal transduction through cGMP, in particular impotence, pulmonary hypertension, and diabetic renal failure paralysis (no data). Thus, 2-(hydroxymethyl)pyridine was treated wit NaH in THF at room temperature for 30 min and then condensed with 2-chloro-5-(3,4,5-trimethoxyphenylcarbonyl)-4-(3-chloro-4-methoxybenzylamino)pyrimidine (preparation given) in THF at room temperature for 1 h
to give 2-(2-pyridylmethoxy)-5-(3,4,5-trimethoxyphenylcarbonyl)-4-(3-chloro-4-methoxybenzylamino)pyrimidine.

IT 372114-59-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as phosphodiesterase V inhibitors preventive or therapeutic agents for various diseases due to dysfunction of signal transduction through cGMP)

RN 372114-59-5 CAPLUS

CN 5-Pyrimidinecarboxamide, 4-[[(3-chloro-4-methoxyphenyl)methyl]amino]-N-[1-[2-(dimethylamino)acetyl]-4-piperidinyl]-2-(2-pyridinylmethoxy)- (CA INDEX NAME)



L6 ANSWER 49 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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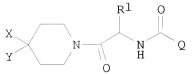


I

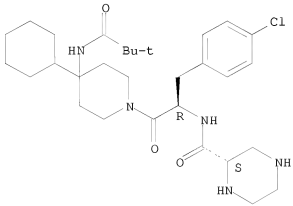
AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepared as melanocortin-4 receptor (MC-4R) agonists. Thus, capsule formulations containing title compound (II) were prepared Representative I activated MC-4R with IC50<1 μM. I are claimed for the treatment of obesity, diabetes, and sexual dysfunction including erectile dysfunction and female sexual dysfunction.

IT 363187-43-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists)

RN 363187-43-3 CAPLUS

CN 2-Piperazinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-cyclohexyl-4-[(2,2-dimethyl-1-oxopropyl)amino]-1-piperidinyl]-2-oxoethyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 50 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

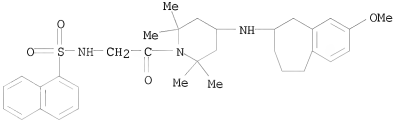
AB The compds. R1R2(NR6)pR5AR3(SO2)sR4 [R1 = (un)substituted (un)saturated C ring, heterocyclyl; R2 = bond, (un)substituted lower alkylene; R3 = piperidinediyl, (CH2)n, CHR7, NH, CO; R7 = indolylmethyl; n = 1-4; R4 = (un)substituted aryl, aralkyl, heterocyclyl; R5 = bond, lower alkylene, (CH2)mCO; m = 0-1; R6 = H, OH; A = N-containing saturated heterocyclylene; p = 0-1; s = 0-1] are prepared N-[[4-[(naphthalen-1-yl)sulfonylaminomethyl]piperidin-1-yl]carbonylmethyl]-2-indolinecarboxamide (263.0 mg) was reacted with borane-Me2S complex in THF under reflux for 2 h and treated with HCl under reflux for 1 h to give 104.8 mg N-(indolin-2-yl)methyl-N-[4-[(naphthalen-1-yl)sulfonylaminomethyl]piperidin-1-yl]ethylamine hydrochloride showing

good inhibitory activity against neuropeptide Y receptor in vitro.

IT 345956-17-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylaminomethylpiperidinylethylamines for antiobesity, antidiabetics, and antihypertensives)

RN 345956-17-4 CAPLUS

CN 1-Naphthalenesulfonamide, N-[2-oxo-2-[2,2,6,6-tetramethyl-4-[(6,7,8,9-tetrahydro-3-methoxy-5H-benzocyclohepten-6-yl)amino]-1-piperidinyl]ethyl]- (CA INDEX NAME)



L6 ANSWER 51 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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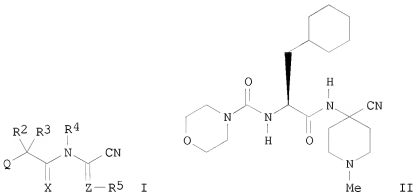


AB Compds. of formula I are claimed [wherein; Q is R1C(=Y)NR4- or R1C(=NR6)NR4- or R1YNR4- or R1C(NR6R8)=N-, where R1 is (cyclo)alkyl(sulfonyl), alkoxy, aryl(sulfonyl) or hetero(aryl)(cyclyl); R2 is H or alkyl; R3 is H, (un)substituted (cyclo)alkyl, alkylene or aryl(alkyl); or R2R3 may form nonarom. carbo- or heterocyclic ring; R4 is H, OH, or alkyl; R5 is bond, H, alkyl optionally interrupted by 1 or 2 O, S, Ph, naphthyl, heterocyclyl, etc.; R6 is H, OH, CN, etc.; R8 is alkyl optionally interrupted by N, O, S, etc.; X, Y are O or S; Z is a spirocyclic junction to certain 4-7 membered ring (substituted)(bridged)(fused)heterocycles]. The compds. are novel, reversible inhibitors of cathepsins S, K, F, L and B, and are useful for treating a variety of autoimmune diseases. Also disclosed are processes for preparing I. Over 100 examples, primarily derived from L-cyclohexylalanine and L-neopentylglycine, are given. Claims cover the

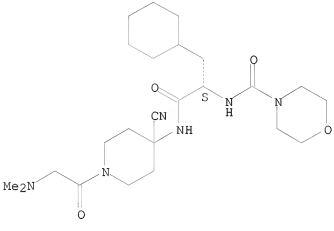
same compds. with unspecified stereochem. For example, L-β-cyclohexylalanine Me ester hydrochloride was neutralized, amidated with 4-morpholinecarbonyl chloride, and saponified with LiOH in aqueous MeOH-THF to give N-(4-morpholinecarbonyl)-L-cyclohexylalanine. This acid derivative was coupled with crude 4-amino-4-cyano-1-methylpiperidine using EDC in the presence of HOBT and N-methylmorpholine in DMF, yielding title compound II. Compds. I inhibited human recombinant cathepsin S in vitro with IC50 values of 100 μM or below.

IT 331278-88-7P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(2-dimethylaminoacetyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of cysteine proteases)

RN 331278-88-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-[2-(dimethylamino)acetyl]-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 52 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB Cathepsin K (EC 3.4.22.38), a cysteine protease of the papain superfamily, is predominantly expressed in osteoclasts and has been postulated as a target for the treatment of osteoporosis. Crystallog. and structure-activity studies on a series of acyclic ketone-based inhibitors of cathepsin K have led to the design and identification of two series of cyclic ketone inhibitors. The mode of binding for four of these cyclic and acyclic inhibitors to cathepsin K is discussed and compared. All of the structures are consistent with addition of the active site thiol to the ketone of the inhibitors with the formation of a hemithioketal. Cocrystn. of the C-3 diastereomeric 3-amidotetrahydrofuran-4-one analog with cathepsin K showed the inhibitor to occupy the unprimed side of the active site with the 3S diastereomer preferred. This C-3 stereochem. preference is in contrast to the x-ray cocrystal structures of the 3-amidopyrrolidin-4-one inhibitors which show these inhibitors to prefer binding of the 3R diastereomer. The 3-amidopyrrolidin-4-one inhibitors were bound in the active site of the enzyme in two alternate directions. Epimerization issues associated with the labile α-amino ketone diastereomeric center contained within these inhibitor classes has proven

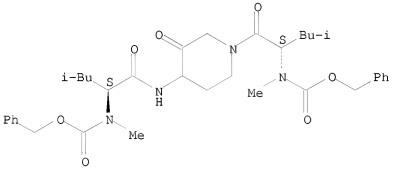
to limit their utility despite promising pharmacokinetics displayed in both series of compds.

IT 330975-08-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic ketone inhibitors of cysteine protease cathepsin K)

RN 330975-08-1 CAPLUS

CN Carbamic acid, methyl[(1S)-3-methyl-1-[[4-[[(2S)-4-methyl-2-[methyl[(phenylmethoxy)carbonyl]amino]-1-oxopentyl]amino]-3-oxo-1-piperidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 53 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

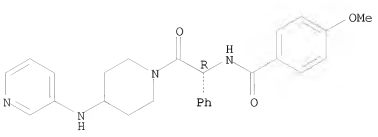
AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 represents a 5- or 6-membered aromatic carbon ring optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5 or 6 membered carbocyclic or heterocyclic ring or substituted at the position alpha to X-X; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)saturated, mono- or polycyclic, homo- or heterocyclic group; Lp is a lipophilic organic group; D is a hydrogen bond donor group; n = 0-2] were prepared for use as serine protease inhibitors. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 1-(3-amino-2-naphthoyl-D-phenylglycinyl)-4,4'-bispiperidine was prepared and shown to double the prothrombin time at a concentration of 26 μM.

IT 313489-54-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as serine protease inhibitors)

RN 313489-54-2 CAPLUS

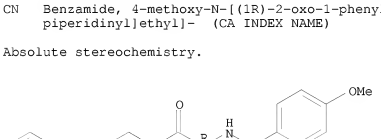
CN Benzamide, 4-methoxy-N-[(1R)-2-oxo-1-phenyl-2-[4-(3-pyridinylamino)-1-piperidinyl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 54 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 represents a 5- or 6-membered aromatic carbon ring optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5 or 6 membered carbocyclic or heterocyclic ring; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)saturated, mono- or polycyclic, homo- or heterocyclic group; Lp is a lipophilic organic group; D is a hydrogen bond donor group; n = 0-2] were prepared for use as serine protease inhibitors. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 1-(3-amino-2-naphthoyl-D-phenylglycinyl)-4,4'-bispiperidine was prepared and shown to double the prothrombin time at a concentration of 26 μM. [This abstract record is one of 2 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]
IT 313489-54-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as serine protease inhibitors)
RN 313489-54-2 CAPLUS
CN Benzamide, 4-methoxy-N-[(1R)-2-oxo-1-phenyl-2-[4-(3-pyridinylamino)-1-piperidinyl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 55 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

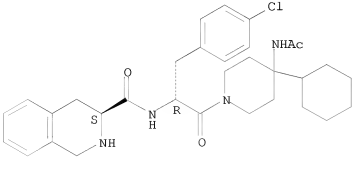
AB Piperidine derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CHRb)n-cycloalkyl, -aryl, -heteroaryl, -O(CHRb)naryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepared as agonists of the human melanocortin receptors, in particular, the human melanocortin-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Thus, II trifluoroacetate, prepared by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]piperidine trifluoroacetate (preparation given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.

IT 312638-63-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine amino acid derivs. as melanocortin-4 receptor agonists)

RN 312638-63-4 CAPLUS

CN 3-Isoquinolinecarboxamide, N-[(1R)-2-[4-(acetylamino)-4-cyclohexyl-1-piperidinyl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-1,2,3,4-tetrahydro-, hydrochloride (1:1), (3S)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 56 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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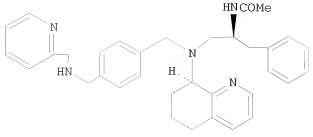

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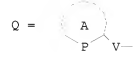
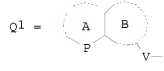




AB Title compds. {YW(X)(Z)(CR1R2)nArCR3R4N(R5)(CR6R7)qR8; W = N, Y is void; WY = CH; R1 to R7 may be the same or different and are independently selected from H, straight, branched or cyclic C1-6 alkyl; R8 = substituted heterocyclic group or a substituted aromatic group; Ar = aromatic or heteroarom. ring each optionally substituted at single or multiple, non-linking positions with electron-donating or withdrawing groups; n and q are independently = 0-2; X = Q, Q1; A = optionally substituted, saturated or unsatd. 5 or 6-membered ring; P = optionally substituted carbon atom, optionally substituted nitrogen atom, sulfur or oxygen atom; B = optionally substituted 5 to 7-membered ring; Ring A and Ring B in the above formula can be connected to the group W from any position via the group V; V = bond, (CH2)m, CO; m = 0-2; Z = H, optionally substituted C1-6 alkyl group, C0-6 alkyl group substituted with an optionally substituted aromatic or heterocyclic group, optionally substituted C0-6 alkylamino, C3-7 cycloalkylamino group, optionally substituted carbonyl group or sulfonyl], pharmaceutically acceptable acid addition, salts, metal complexes, stereoisomers, isomer mixts., and pharmaceutical composition are prepared

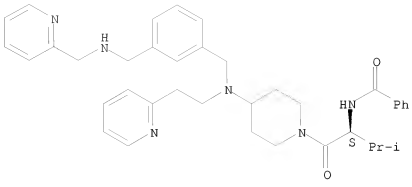
Title compds. are having protective effects against infection by HIV through binding to chemokine receptors, including CXCR4 and CCR5 and inhibiting the subsequent binding of their natural ligands. Thus, the title compound I was prepared and tested for inhibition of HIV-1 NL4.3 or IIIB replication in MT-4 cells and exhibited EC50's of less than 20μg/mL.

IT 1105999-34-5
RL: PRPH (Prophetic)
(Preparation of heterocyclic derivatives as chemokine receptor antagonists effective against HIV, tumor, and allergy)

RN 1105999-34-5 CAPLUS

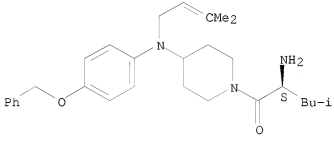
CN Benzamide, N-[(1S)-2-methyl-1-[[4-[[2-(2-pyridinyl)ethyl][[3-[[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]amino]-1-piperidinyl]carbonyl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 57 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Several novel N-type voltage sensitive calcium channel blockers showed high affinity in the IMR32 assay and efficacy in the anti-writhing model. Herein, we describe the design, synthesis, SAR studies, biol. data, physicochem. properties and pharmacokinetics of this 4-piperidinylaniline series.
IT 250237-01-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(design, synthesis, SAR studies of 4-piperidinylaniline analogs with analgesic activity)
RN 250237-01-5 CAPLUS
CN 1-Pentanone, 2-amino-4-methyl-1-[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

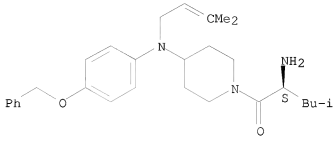
Absolute stereochemistry.



L6 ANSWER 58 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Selective N-Type Voltage Sensitive Calcium Channel (VSCC) antagonists have shown utility in several models of pain and ischemia. The authors report the synthesis and biol. activity of a series of 4-aminopiperidine derivs. with activity at N-type calcium channels. Several novel compds. with improved properties are disclosed.
IT 250237-01-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of aminopiperidine derivs. as N-type calcium channel antagonists)
RN 250237-01-5 CAPLUS

CN 1-Pentanone, 2-amino-4-methyl-1-[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 59 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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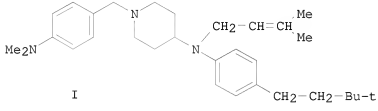


I

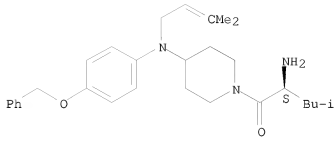
AB Our drug discovery efforts for N-type calcium channel blockers in the 4-piperidinylaniline series led to the discovery of an orally active analgesic agent I. I showed high affinity to functionally block N-type calcium channels (IC50=0.7 μM in the IMR32 assay) and exhibited high efficacy in the anti-writhing analgesia test with mice (ED50=12 mg/kg by po and 4 mg/kg by iv). In this report, the rationale for the design, synthesis, biol. evaluation, and pharmacokinetics of this series of blockers is described.

IT 250237-01-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylanilines as calcium channel blockers and analgesics)

RN 250237-01-5 CAPLUS

CN 1-Pentanone, 2-amino-4-methyl-1-[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 60 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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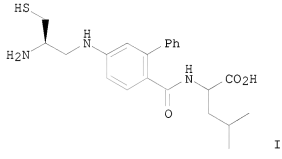


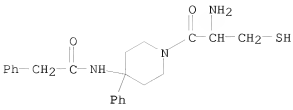
I

AB A method for inhibiting the growth of a fungal pathogen comprises contacting the pathogen with a compound, e.g., (R70)2NCH[(CH2)nR]C(Xa)NHCHR72C(Xb)NHCHR73C(Xc)NHCHR10CO2R11 [Xa, Xb, Xc = O, H2; R = SR1, SOR111, SO2R111; R1 = H, alkyl, alkenyl, aryl, acyl; R10 = alkyl, alkenyl, alkynyl, aryl, cycloalkyl, hydroxyalkyl, amino acid sidechain, etc.; R11 = H, blocking group, pharmaceutically acceptable salt; R10R11 = atoms to form 5-7 membered ring; R111 = alkyl, alkenyl, (CH2)mR7; R70 = H, alkyl, alkenyl, alkynyl, aryl, acyl, amino acid sidechain, etc.; R72, R73 = H, alkyl, aryl, heteroaryl, amino acid sidechain, (CH2)mR7, etc.; m, n = 0-4], which inhibits prenyl transferase activity with MIC50<25 μg/mL. Thus, title compound (I) (solution phase preparation given) inhibited GGTase with IC50<10 nM.

IT 256369-44-5
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of peptides, peptidomimetics, and nonpeptides as medical and agrochem. antifungals)

RN 256369-44-5 CAPLUS

CN Benzeneacetamide, N-[1-(2-amino-3-mercapto-1-oxopropyl)-4-phenyl-4-piperidinyl]- (CA INDEX NAME)



L6 ANSWER 61 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB Peptides R8NH(CR6R7)f(CH2)e-M-(CHR5)d(CH2)cCONR1CH[(CH2)a-G]CONR2CH[(CH2)b-J]CO-L [R1 = H, alkyl; L = (un)substituted aza heterocyclyl or aza heterocyclylamino or -methylamino; G, J = -O(CH2)kR17 (k = 0-2, R17 = H, halo, aryl, hetaryl, alkyl, alkoxy), (un)substituted Ph, pyridyl, naphthyl, indolyl, imidazolyl, thienyl, or benzothienyl; a, b, c = 0-2; d, f = 0 or 1; e = 0-3; R5-R8 = H or (un)substituted alkyl; M = arylene, hetarylene, O, S, or ethylene which is optionally substituted by alkyl, arylalkyl, or hetarylalkyl] were prepared for treating medical disorders resulting from a deficiency in growth hormone. Thus, (2E)-5-amino-5-methylhex-2-enoic acid N-[(1R)-1-[N-[(1R)-1-benzyl-2-[4-[(dimethylamino)methyl]piperidin-1-yl]-2-oxoethyl]-N-methylcarbamoyl]-2-(2-naphthyl)ethyl]-N-methylamide was prepared via amidation of (2E)-5-[(tert-butoxycarbonyl)amino]-5-methylhex-2-enoic acid, followed by cleavage of the protecting group with trifluoroacetic acid.

IT 254905-32-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

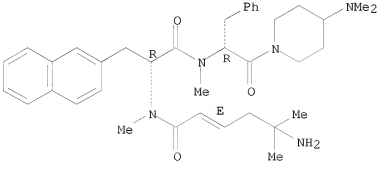
(preparation of peptide derivs. with growth hormone releasing properties)

RN 254905-32-3 CAPLUS

CN 4-Piperidinamine, 1-[N-[(2E)-5-amino-5-methyl-1-oxo-2-hexen-1-yl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N-methyl-D-phenylalanyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L6 ANSWER 62 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB The title compds. R1ANR2CH(DER3)COJR4 [R1 = alkyl, etc.; A = CO, etc.; R2 = H, (un)substituted alkyl; D = alkylene, etc.; E = OCO, etc.; R3 = heterocyclic ring, etc.; J = O, etc.; R4 = alkyl, etc.] are prepared The title compds. are useful as preventives and/or remedies for brain infarction, transient ischemic attack, cerebrospinal failure following heart operation, spinal vascular failure, stress hypertension, neurosis, epilepsy, asthma, frequent urination, etc., or analgesics. In an in vitro

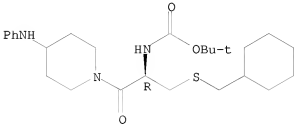
test (using cells) for N type calcium channel inhibiting activity, (2R)-N-(1-benzylpiperidin-4-yl)-3-cyclohexylmethylthio-2-((4R)-3-tert-butoxycarbonylthiazolidin-4-ylcarbonylamino)propanamide at 3 μM gave 95% inhibition of calcium inflow. Formulations containing the title compds. are given.

IT 253306-27-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as N type calcium channel inhibitors)

RN 253306-27-3 CAPLUS

CN Carbamic acid, [(1R)-1-[[(cyclohexylmethyl)thio]methyl]-2-oxo-2-[4-(phenylamino)-1-piperidinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 63 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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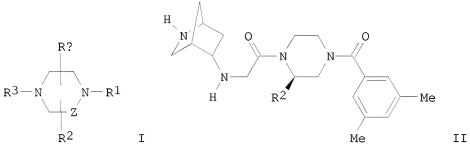


AB Title compds. [I;R1 = C(:X)(CHRc')lA1; A1 = (un)substituted Ph, -naphthyl, -heteroaryl, etc.; R2 = (CH2)uA2; A2 = (un)substituted Ph, -naphthyl; R3 = [C(:X)]m(CHRc)yR; R = e.g., (di)azabicycloalkylamino having ring-N substituent G; G = H, alkyl, acyl, arylmethyl, etc.; Rc = H, alkyl, (CH2)1-4R4; R4 = ORa, NRaRb, CO2Ra, imidazolyl, etc.; Ra,Rb = H, alkyl, Ph, etc.; Rc' = H, (CH2)nORa; X = O, H2, NH, etc.; Z = (CH2)0-2; u,n,l = 0-2; m = 1 and y = 1-3; m = 2 and y = 0] were prepared Thus, (R)-1-bromoacetyl-2-(3,4-dichlorophenyl)-4-(3,5-dimethylbenzoyl)piperazine was aminated by 1,1-dimethylethyl 5-amino-2-azabicyclo[2.2]heptane-2-carboxylate (preparation each given) to give title compound II (R2 = 3,4-dichlorophenyl). Data for biol. activity of I were given.

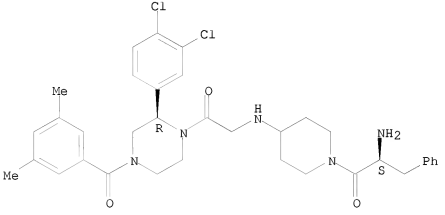
IT 207404-84-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,4-diacyl piperazines and analogs as neurokinin antagonists)

RN 207404-84-0 CAPLUS

CN 1-Propanone, 2-amino-1-[4-[[2-[(2R)-2-(3,4-dichlorophenyl)-4-(3,5-dimethylbenzoyl)-1-piperazinyl]-2-oxoethyl]amino]-1-piperidinyl]-3-phenyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 64 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB In this article, the rationale for the design, synthesis, and biol. evaluation of a series of N-type voltage-sensitive calcium channel (VSCC) blockers is described. N-Type VSCC blockers, such as ziconotide, have shown utility in several models of stroke and pain. Modification of the previously reported lead led to several 4-(4-benzyloxylphenyl)piperidine structures with potent in vitro and in vivo activities. In this series, the most interesting compound, (S)-2-amino-1-{4-[(4-benzyloxy-phenyl)-(3-methyl-but-2-enyl)-amino]-piperidin-1-yl}-4-methyl-pentan-1-one (I), blocked N-type calcium channels (IC50 = 0.67 μM in the IMR32 assay) and was efficacious in the audiogenic DBA/2 seizure mouse model (ED50 = 6 mg/kg, i.v.) as well as the antiwrithing model (ED50 = 6 mg/kg, i.v.). Whole-cell voltage-clamp electrophysiol. expts. demonstrated that compound I blocked N-type Ca2+ channels and Na+ channels in superior cervical ganglion neurons at similar concns. Compound I, which showed superior in vivo efficacy, stands out as an interesting lead for further development of neurotherapeutic agents in this series.

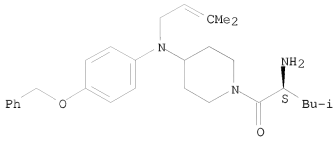
IT 250237-01-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 4-benzyloxyaniline analogs as neuronal N-type calcium channel blockers with improved anticonvulsant and analgesic properties)

RN 250237-01-5 CAPLUS

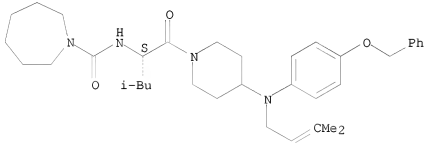
CN 1-Pentanone, 2-amino-4-methyl-1-[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 65 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
AB Selective N-Type Voltage Sensitive Calcium Channel (VSCC) antagonists have shown utility in several models of pain and ischemia. The authors report the structure-activity relationship at the proximal Ph group in a series of non-peptidyl VSCC blockers.
IT 247130-18-3, PD 181283
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity relationship at the proximal Ph group in a series of non-peptidyl N-type calcium channel antagonists)
RN 247130-18-3 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[4-[(3-methyl-2-buten-1-yl)[4-(phenylmethoxy)phenyl]amino]-1-piperidinyl]carbonyl]butyl]-(CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 66 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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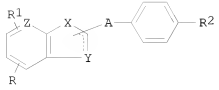
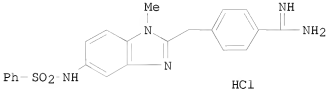


I



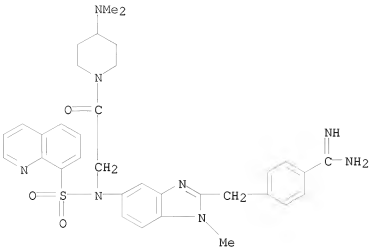
HCl II

AB Title compds. [I; R = 5-C6H5SO2NH, 6-C6H5SO2NH, 5-C6H5NHSO2, 5-C6H5SO2N(CH2COOEt), 5-C6H5SO2N(CH3), 5-C6H5N(CH2CH2CH2COOEt)CO, 5-C6H5, CH3N(C6H5)CO, 8; R1 = H, 7-CH3, 3-Br, 3-EtO; R2 = C(:NH)NH2; A = CH2, NH; X = CH, MeN, EtOCOCH2CH2N, O, S, NCH2CO2H; Y = N, CH, CH:CH; Z = CH, N; dotted bond = single, double in relation to X; A is attached at 2,or 8 position depending on the heterocyclic ring] and their tautomers, stereoisomers, mixts. and their physiol. compatible salts with inorg. or organic acids or bases are prepared and title compds in which R2 is a cyano group, present valuable intermediate products for the production of the remaining compds. of the general formula I, with R2 is amidino, which have valuable pharmacol. properties, especially an antithrombotic activity. Thus, the title compound II was prepared

IT 236415-15-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of five-membered benzo-condensed heterocycles as antithrombotics)

RN 236415-15-9 CAPLUS

CN Benzenecarboximidamide, 4-[[5-[[2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl](8-quinolinylsulfonyl)amino]-1-methyl-1H-benzimidazol-2-yl]methyl]-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

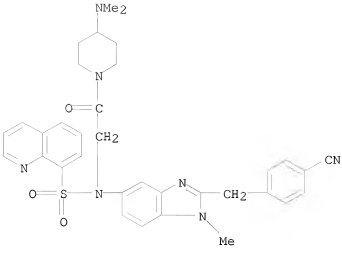
L6 ANSWER 67 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB Approx. 300 antithrombotic title compds. such as 4-[5-[N-(8-quinolylsulfonyl)-N-(carboxymethyl)amino]-1-methyl-1H-benzimidazol-2-ylmethyl]benzamidine hydrochloride (I), 4-[5-[N-(benzenesulfonyl)-N-[2-(dimethylamino)ethyl]amino]-1-benzyl-1H-benzimidazol-2-ylmethyl]benzamidine dihydrochloride, 4-[5-[N-(3-carboxypropionyl)-N-(cyclopentyl)amino]-1-methyl-1H-benzimidazol-2-ylmethyl]benzamidine hydrochloride (II), and 4-[5-[N-(8-quinolylsulfonyl)-N-(carboxymethyl)amino]-1-methyl-1H-benzothiazol-2-ylmethyl]benzamidine hydrochloride were prepared by standard methods. The ED200 in μM for I was 0.92 and for II was 0.82. Formulations for the antithrombotics were given.

IT 237752-17-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antithrombotic activity of benzimidazolylmethylbenzamidines)

RN 237752-17-9 CAPLUS

CN 8-Quinolinesulfonamide, N-[2-[(4-cyanophenyl)methyl]-1-methyl-1H-benzimidazol-5-yl]-N-[2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl]- (CA INDEX NAME)



L6 ANSWER 68 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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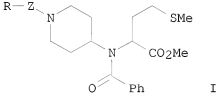


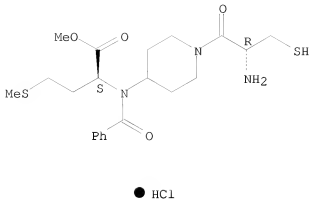
AB The design and synthesis of a family of CA1A2X peptidomimetics as inhibitors of Ras farnesyltransferase (IRFTase) are reported. These inhibitors lack the central dipeptide A1A2 in the key carboxyl terminus sequence of farnesylated proteins. Using the CVFM peptide as a starting point, the authors' design led to the synthesis of a non-peptidic scaffold dipeptide mimetic bearing cysteine and methionine residues, considered to be essential recognition elements. Replacement of the cysteinyl residue by heterocycles recognized the role of zinc in the active site of the enzyme and helped to circumvent the metabolic instability of amino acids. Pharmacol. evaluations of these methionine-containing compds. I [Z = H, CO, CH2; R = CH(NH2)CH2SH, L- and D-4-thiazolidinyl, 4-thiazolyl, 4-imidazolyl] for enzymic and antiproliferative activity suggest a new class of potent non-peptidic IRFTase.

IT 227314-71-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of methionine-based, non-peptidic inhibitors of Ras farnesyltransferase)

RN 227314-71-8 CAPLUS

CN L-Methionine, N-[1-[(2R)-2-amino-3-mercapto-1-oxopropyl]-4-piperidinyl]-N-benzoyl-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 69 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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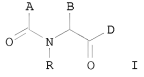
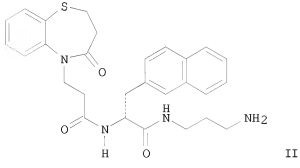




AB The title compds. [I; A = a lipophilic group comprising an aliphatic bridging group; B = a lipophilic group; D = a group having at least one (un)substituted amino group; R = H, alkyl, cycloalkyl] and their pharmaceutically acceptable salts and individual isomers which have growth hormone releasing activity in humans or animals and are useful, e.g., in treating osteoporosis, bone fractures, wounds or burns, were prepared E.g., a 2-step synthesis of amide (1R)-II.HCl which showed growth hormone (GH) activity < 10-8 M, was given.

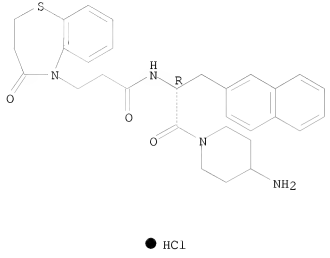
IT 220976-80-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel amide derivs. having growth hormone releasing activity)

RN 220976-80-7 CAPLUS

CN 1,5-Benzothiazepine-5(2H)-propanamide,

N-[(1R)-2-(4-amino-1-piperidinyl)-1-(2-naphthalenylmethyl)-2-oxoethyl]-3,4-dihydro-4-oxo-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 70 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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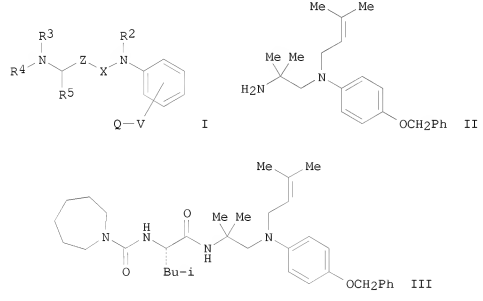


AB The invention provides compds. that block calcium channels. In particular, the invention claims compds. I [Z = CH2 or CO; X = cycloalkylene, (un)substituted heterocycloalkylene, imino or iminoalkylene, certain piperidinediyl or pyrrolidinediyl radicals or their alkylene derivs.; Q = H, (un)substituted aryl, heteroaryl, cycloalkyl, alkyl, heterocycloalkyl; V = O(CH2)n or (CH2)nO, O, (CH2)n, CH:CH, NH(CH2)n or (CH2)nNH or derivs.; R2 = H, alkenyl, cycloalkenyl, (un)substituted Ph, alkyl, cycloalkyl, or Ph; R3 = H, alkyl, alkenyl; R4 =

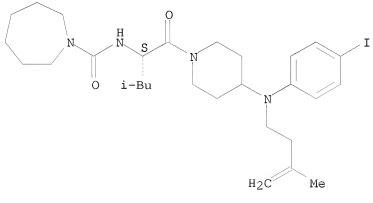
H, cyclo-(CH2)mNCO, alkyl, alkenyl, (un)substituted Ph, heteroaryl, or cycloalkyl; or NR3R4 = 5- to 7-membered ring with an optional addnl. heteroatom; R5 = alkyl, (un)substituted Ph or heteroaryl; m = 1-3; n = 0-3] and their pharmaceutically acceptable salts, esters, amides, and prodrugs. The invention also provides methods of using the compds. to treat stroke, cerebral ischemia, head trauma, or epilepsy, and to pharmaceutical compns. that contain the compds. Over 50 synthetic examples are given, and these plus a large number of addnl. invention compds. are specifically claimed. For instance, N-BOC-α-aminoisobutyric acid underwent amidation with 4-benzyloxyaniline, followed by reduction of the amide with diborane, N-alkenylation with 4-bromo-2-methyl-2-butene, and acidic deprotection to remove BOC, to give intermediate II. In a sep. preparation, H-Leu-OCH2Ph was treated with triphosgene and hexamethylenamine, then deprotected, to give Hac-Leu-OH (III; Hac = hexamethylenaminocarbonyl). Coupling of II with III using HBTU and DIPEA in DMF gave title compound IV. The latter blocked calcium flux through N-type Ca2+ channels in IMR-32 neuronal tumor cells in vitro, with IC50 of 0.26 μM. Selected compds. gave 20-100% protection of mice from tonic seizures in a sound chamber, at doses of 10-30 mg/kg i.v.

IT 220741-65-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(alkynylation; preparation of aniline derivs. as calcium channel blockers)

RN 220741-65-1 CAPLUS

CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-1-[[4-[(4-iodophenyl)(3-methyl-3-buten-1-yl)amino]-1-piperidinyl]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



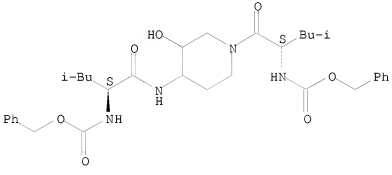
L6 ANSWER 71 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB To design more potent inhibitors of cathepsin K, the authors incorporated a 1,3-bis(Cbz-Leu-amino)-2-propanone inhibitor template into conformationally constrained ring systems. Introduction of a conformational constraint was used to capture bioactive orientations of mols. A variety of structure-activity relations are reported. Incorporation of the sulfonamide into the peptidomimetic gave the potent 4-phenoxybenzenesulfonamide derivative This modification has removed most of the structural liabilities commonly associated with peptide amide linkages.

IT 203501-30-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(conformationally constrained 1,3-diamino ketones as potent inhibitors

of the cysteine protease cathepsin K)
RN 203501-30-8 CAPLUS
CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-piperidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 72 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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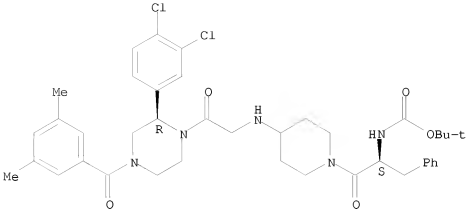
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; X = O, (H,H), S, imino; Q = (CH2)n; n, q, u = 0-2; m = 1, p = 1-3; or m = 2 and p = 0; Q1 = (CH2)uAr2; Rc = H, (substituted) alkyl; Rc1 = H, alkyl, hydroxyalkyl, etc.; Ar1 = (substituted) heteroaryl, Ph, fluorenyl, naphthyl, etc.; Ar2 = (substituted) heteroaryl, Ph, naphthyl; Z = specified (substituted) aza(bi)cycloalkylamino, aza(bi)cycloalkyloxy, aza(bi)cycloalkylmethyl, etc.; with provisos], were prepared Thus, 1-(3,5-dimethylbenzoyl)-3(R)-3,4-dichlorophenylpiperazine (preparation given) was treated with ClCOCH2CH2Br and Et3N in CH2Cl2 to give the bromopropionyl derivative, which in EtOH was treated with (1S,4S)-N-tert-butoxycarbonyl-2,5-diazabicyclo[2.2.1]heptane and Et3N to give the coupling product which was deprotected and coupled with BOC-D-Phg-OH using HOBT/DEC/Et3N in CH2Cl2 to give title compound (II). I inhibited NK1 binding by 0-100% at 1 μM.
IT 207404-75-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diacylpiperazine derivs. as neurokinin antagonists)
RN 207404-75-9 CAPLUS
CN Carbamic acid, [(1S)-2-[4-[[2-[(2R)-2-(3,4-dichlorophenyl)-4-(3,5-dimethylbenzoyl)-1-piperazinyl]-2-oxoethyl]amino]-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 73 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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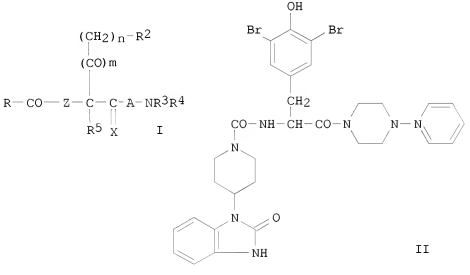


AB The invention concerns modified amino acids of general formula I [A = bond, CX; Z = CH2, NR1; R1 = H, alkyl, phenyl-alkyl; X = O, H,H; n = 1-2; m = 0-1; R = (substituted)alkyl; R2 = Ph, (substituted)(hetero)(bi)cycle; R3 = H, (substituted)alkyl, Ph, pyridinyl; R4 = H, (substituted)alkyl; R3R4= (hetero)cycle; R5 = H, alkyl, alkoxycarbonyl, PhCH2], pharmaceuticals containing these compds., their use and the method for their production, as well as their use for the production and purification of antibodies and as marked compds. in RIA and ELISA assays and as diagnostic or analytic auxiliary agents in neurotransmitter research. Thus, 3,5-dibromo-N2-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II(22%). Title compds. show human calcitonin gene related peptide (CGRP) antagonist activity; in in-vitro binding studies with Sk-N-MC-cells, I had IC50 ≤10000 nM, and in

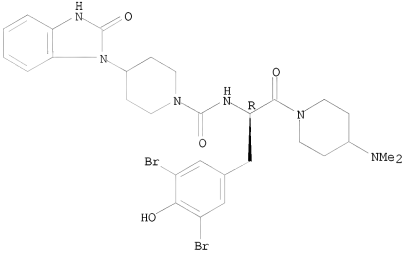
the same system, had CGRP-antagonist activity at doses from 10-11 to 10-6 M.

IT 204695-54-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compns.)

RN 204695-54-5 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl]-4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 74 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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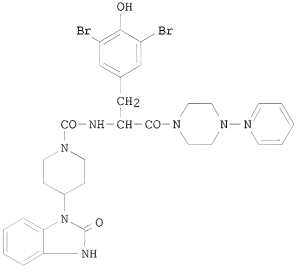


II

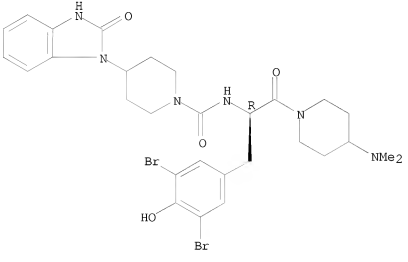
AB Title compds. RCOZCR1R2C(:X)ANR3R4 [(I); R = (substituted) alkyl; R1 = H, alkyl, PhCH2; R2 = (CO)m(CH2)nR5; m = 0, 1; n = 1, 2; R5 = Ph, heterocycle; X = O, (H,H); Z = CH2, NR6; R6 = H, alkyl, phenyl-alkyl; A = bond, proline; R3 = H, substituted alkyl, Ph, pyridinyl; R4 = H, substituted alkyl; NR3R4 = (substituted) heterocycle], useful as calcitonin gene-related peptide (CGRP) antagonists, were prepared Thus, 3,5-dibromo-N2-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II (22%). In in-vitro binding studies with human CGRP-receptors, I had IC50 ≤10000 nM; in CGRP-antagonist in vitro tests, I was effective at doses from 10-11 to 10-5 M.

IT 204695-54-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compns.)

RN 204695-54-5 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-[4-(dimethylamino)-1-piperidinyl]-2-oxoethyl]-4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 75 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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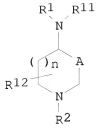

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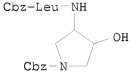
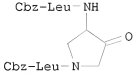


II



III

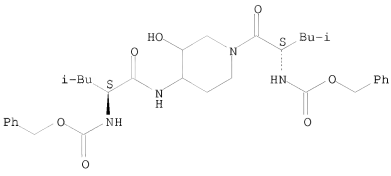
AB Title heterocycles I [A = CO, CH(OH); R11, R12, R9, R6 = = H, C1-6 alkyl, C3-6 cycloalkyl-C0-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl; R1 = R4R10NCHR3Z, ARCHR9CO, 4-(Ph-Y)C6H4CO, dibenzofuran-2-sulfonyl; R2 = any group R11, R5CO, R5CS, R5SO2, R5O2C, R5R10NCO, R5R10NCS, adamantyl-CO, R6R7NCHR3-Z; R3 = H, C2-6 alkenyl, C2-6 alkynyl, Het, Ar, C1-6 alkyl (un)substituted by OR10, SR10, NR102, R10NCO2R5, CO2R10, CO2NR102, NC:NHNH2, Het, Ar; R4, R7 = any group R11, R5CO, R5CS, R5SO2, R5O2C, R5R10NCO, R5R10NCS, R10HNCHR10CO, R5O2CNR10CHR10CO; R5 = C3-6 cycloalkyl-C0-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl, Ar-C0-6 alkoxy, Het-C0-6 alkoxy, C1-6 alkyl (un)substituted by OR10, SR10, NR102, R10NCO2R5, CO2R10, CO2NR102, NC:NHNH2, Het, Ar; NR6R7 = pyrrolidino, piperidino, morpholino; R10 = H, C1-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl; Y = bond, O; Z = CO, CH2; n = 0-2; Ar = aryl, Het = heterocyclyl] or a pharmaceutically acceptable salt thereof, are inhibitors of cysteine proteases, particularly cathepsin K, and are useful in the treatment of diseases in which inhibition of bone loss is a factor. Thus, coupling of 1-tert-butoxycarbonyl-trans-3-amino-4-hydroxypyrrolidine (preparation given) with Cbz-Leu-OH (Cbz = PhCH2O2C), followed by deprotection with HCl in EtOAc and further coupling with Cbz-Leu-OH gave trans-pyrrolidinol II. Jones oxidation of II gave desired title compound III.

IT 203501-30-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic peptide derivs. as cysteine protease inhibitors)

RN 203501-30-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-piperidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 76 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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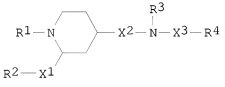


I

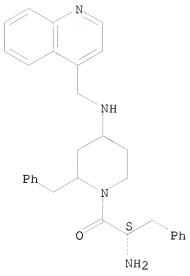
AB The invention relates to the use of substituted piperidineamines I or of a pharmaceutically utilizable salt thereof, in which R1 is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an α-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl; R2 is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical; R3 is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl; R4 is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical; X1 is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group; X2 is alkylene, carbonyl or a direct linkage; and X3 is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by Ph, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than α; for producing pharmaceutical products for the treatment of social phobia. Thus, the preparation and formulation of (2R,2S)-2-benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine as p antagonists for treating social phobia, are reported.

IT 200641-29-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of substituted piperidineamines as p antagonists for treating social phobia)

RN 200641-29-8 CAPLUS

CN 1-Propanone, 2-amino-3-phenyl-1-[2-(phenylmethyl)-4-[(4-quinolinylmethyl)amino]-1-piperidinyl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 77 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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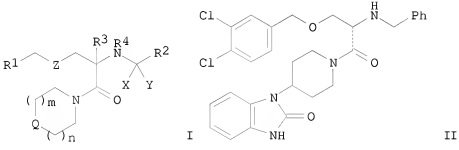
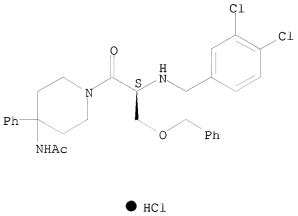


AB Title compds. I [m = 0-2; n = 0, 1; with the proviso that m + n = 1 or 2; R1 = Ph, naphthyl, Ph2CH, PhCH2, where the naphthyl or any Ph moiety may be substituted; R2 = H, Ph, heteroaryl such as indazolyl, thienyl, furanyl, pyridyl, thiazolyl, tetrazolyl, quinolinyl, naphthyl, Ph2CH, PhCH2, wherein each heteroaryl, the naphthyl and any Ph moiety may be substituted; R3, R4 = independently H, C1-6 alkyl; R3R4 = C1-3 alkylene chain; Q = CR5R6, NR5; X = Y = H; XY = O; Z = bond, O, S, S(O), SO2, NR7 or CR7R8; R7, R8 = independently H, C1-6 alkyl] or pharmaceutically acceptable salts thereof are of particular use in the treatment or prevention of pain, inflammation, migraine, emesis and postherpetic neuralgia. Thus, coupling of (S)-2-tert-butoxycarbonylamino-3-(3,4-dichlorobenzyloxy)propionic acid with 4-(2-keto-1-benzimidazolinyl)piperidine, followed by acidic deprotection and reductive benzylation with benzaldehyde and sodium borohydride gave serine derivative II as its HCl salt. The compds. prepared here are active with IC50 at the NK1 receptor of less than 1 μM.

IT 199103-96-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of serine derivs. useful as tachykinin antagonists)

RN 199103-96-3 CAPLUS
CN Acetamide, N-[1-[(2S)-2-[[(3,4-dichlorophenyl)methyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-4-phenyl-4-piperidinyl]-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 78 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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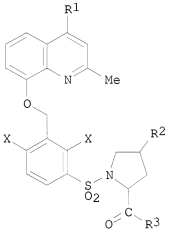


I

AB Benzenesulfonyl pyrrolidine derivs. I (X = halo; R1 = H, alkyl; R2 = H, OH; R3 = substituted 1-piperazinyl, 4-piperidinylalkoxy, etc.) were prepared as bradykinin receptor antagonists. Thus, I (X = Cl, R1, R2 = H, R3 = 1-piperazinyl) was prepared by amidation of N-[[3-[(2-methylquinolin-8-yl)oxymethyl]-2,4-dichlorophenyl]sulfonyl]-L-proline with piperazine and shown to have 100 % bradykinin receptor antagonist activity.

IT 193543-62-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

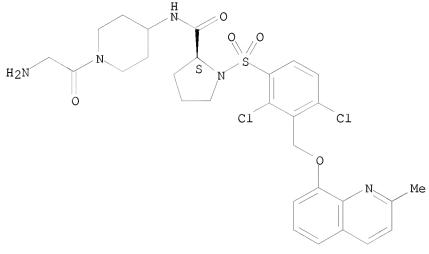
(benzenesulfonyl pyrrolidine derivs. as bradykinin receptor antagonists)

RN 193543-62-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, N-[1-(2-aminoacetyl)-4-piperidinyl]-1-[[2,4-dichloro-3-[[(2-methyl-8-quinolinyl)oxy]methyl]phenyl]sulfonyl]-, hydrochloride (1:2), (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

●2 HCl

L6 ANSWER 79 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB Arylsulfonamido-substituted hydroxamic acids HONHCOCR1R2N(CH2R)SO2Ar (Ar = carbocyclic or heterocyclic aryl; R, R1 = H, alkyl, aryl, etc.; R2 = H, alkyl; R and R1 or R1 and R2 may form a ring) or their pharmaceutically acceptable prodrug derivs. or salts were prepared as antitumor agents. Thus, N-hydroxy-2(R)-[(4-methoxybenzenesulfonyl)(3-picolyl)amino]-3-methylbutanamide was prepared from D-valine, 4-methoxybenzenesulfonyl chloride, 3-picolyl chloride hydrochloride, and O-tert-butylhydroxylamine hydrochloride.

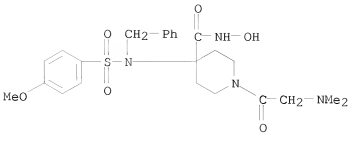
IT 161314-09-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of arylsulfonamido-substituted hydroxamic acids as matrix-degrading metalloproteinase inhibitors)

RN 161314-09-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[2-(dimethylamino)acetyl]-N-hydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L6 ANSWER 80 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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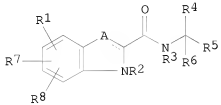
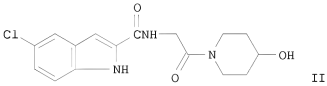


I



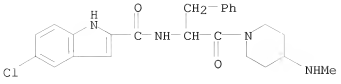
II

AB The title compds. [I; A = CH, C(halo), N, etc.; R1, R7, R8 = H, halo, CN, etc.; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, heterocyclylalkyl, etc.; R5 = H, Me, Et, Pr, CH2OH, (CH2)2OH; R6 = COOH, C1-8 alkoxycarbonyl, benzyloxycarbonyl, etc.], useful to treat diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals, were prepared Thus, coupling 4-hydroxypiperidine with [(5-chloro-1H-indole-2-carbonyl)amino]acetic acid in the presence of hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (DEC) in DMF/CH2Cl2 afforded 68% II. In general, compds. I were effective at 0.1-15 mg/kg/day.

IT 186429-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted N-(indole-2-carbonyl)glycinamides and derivs. as glycogen phosphorylase inhibitors)

RN 186429-69-6 CAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[4-(methylamino)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (CA INDEX NAME)



L6 ANSWER 81 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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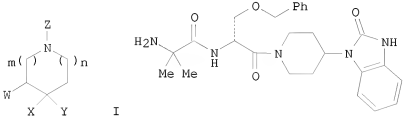


I II

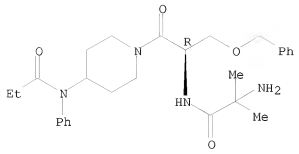
AB Title compds. I [Z = COCR1R2cLCOANR4R5; L = NR6, O, CH2; W = H; W and X = benzo fusion substituted with 0-3 R3a, TR3b, or R12; Y = H, C1-6 alkyl, C4-10 cycloalkyl, aryl-K, phenyl-(C1-6alkyl)-K, thienyl-(C1-6 alkyl)-K substituted with 0-3 R3a, R3b, or R12; K = bond, O, S(O)m, NR2a; X = OR2, R50MN(Aryl), R8R9NCO, R2bO2C, (un)substituted carbo- or heterobicyclic ring; R1 = (un)substituted C1-10 alkyl, aryl, etc.; R2c = H, C1-6 alkyl, C3-7 cycloalkyl; CR1R3c = (un)substituted C3-8 ring; R2 = H, C1-6 alkyl, C3-7 cycloalkyl; R2a = H, C1-6 alkyl; R2b = H, C1-8 alkyl, C1-8 halogenated alkyl, C3-8 cycloalkyl, alkylaryl, aryl; R3a, R12 = independently H, halo, Me, OMe, CF3; T = bond, phenylene, 5- or 6-membered heterocycle containing 1-3 hetero atoms; R3b = H, CONR8R9, SO2R8R9, CO2H, CO2(C1-6 alkyl), NR2SO2R9, NR2CONR8R9, NR2SO2NR8R9, NR2COR9, imidazolyl, thiazolyl, tetrazolyl; R4, R5 = independently H, (un)substituted C1-6 alkyl; R6 = H, C1-6 alkyl; R6CR2c = C3-8 ring; R50 = (un)substituted morpholino, piperazino, C3-7 cycloalkyl, C1-6 alkyl; M = CO, SO2; A = bond, Z1(CH2)xCR7R7a(CH2)y; Z1 = NR2, O, bond; R7, R7a = independently H, CF3, Ph, (un)substituted C1-6 alkyl; R8 = H, (un)substituted C1-6 alkyl; R9 = H, (un)substituted C1-6 alkyl, Ph, thiazolyl, imidazolyl, furyl, thienyl], are growth hormone releasing peptide mimics. Heterocyclic dipeptide derivs. I are useful for the treatment and prevention of osteoporosis (no data). Thus, condensation of Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) with 4-(2-oxo-1-benzimidazolinyl)piperidine, followed by deprotection, coupling with BocNHCMe2CO2H, and deprotection with HCl gave dipeptide amide salt II.

IT 185055-81-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of growth hormone-releasing dipeptides)

RN 185055-81-6 CAPLUS

CN Propanamide, 2-amino-2-methyl-N-[(1R)-2-oxo-2-[4-[(1-oxopropyl)phenylamino]-1-piperidinyl]-1-[(phenylmethoxy)methyl]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 82 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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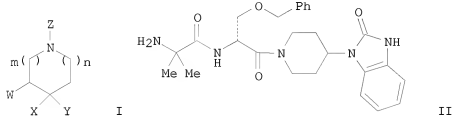


I II

AB Title compds. I [Z = COCR1R2cLCOANR4R5; L = NR6, O, CH2; W = H; W and X = benzo fusion optionally substituted with 1-3 R3a, TR3b, or R12; Y = H, C1-6 alkyl, C3-10 cycloalkyl, aryl optionally substituted with 1-3 R3a, R3b, or R12; X = OR2, R50MN(Aryl), R8R9NCO, R2bO2C, optionally substituted carbobicyclic or heterobicyclic ring; R1 = optionally substituted C1-10 alkyl, aryl, etc.; R2c = H, C1-6 alkyl, C3-7 cycloalkyl; CR1R3c = optionally substituted C3-8 ring; R2 = H, C1-6 alkyl, C3-7 cycloalkyl; R2a = H, C1-6 alkyl; R2b = H, C1-8 alkyl, C1-8 halogenated alkyl, C3-8 cycloalkyl, alkylaryl, aryl; R3a, R12 = independently H, halo, Me, OMe, CF3; T = bond, phenylene, 5- or 6-membered heterocycle containing 1-3 hetero atoms; R3b = H, CONR8R9, SO2R8R9, CO2H, CO2(C1-6 alkyl), NR2SO2R9, NR2CONR8R9, NR2SO2NR8R9, NR2COR9, imidazolyl, thiazolyl, tetrazolyl; R4, R5 = independently H, optionally substituted C1-6 alkyl; R6 = H, C1-6 alkyl; R6CR2c = C3-8 ring; R50 = optionally substituted morpholino, piperazino, C3-7 cycloalkyl, C1-6 alkyl; M = CO, SO2; A = bond, Z1(CH2)xCR7R7a(CH2)y; Z1 = NR2, O, bond; R7, R7a = independently H, CF3, Ph, optionally substituted C1-6 alkyl; R8 = H, optionally substituted C1-6 alkyl; R9 = H, optionally substituted C1-6 alkyl, Ph, thiazolyl, imidazolyl, furyl, thienyl], are growth hormone releasing peptide mimics. Heterocyclic dipeptide derivs. I are useful for the treatment and prevention of osteoporosis. Thus, condensation of Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) with 4-(2-oxo-1-benzimidazolinyl)piperidine, followed by deprotection, coupling with BocNHCMe2CO2H, and deprotection with HCl gave dipeptide amide salt II.

IT 185055-81-6P

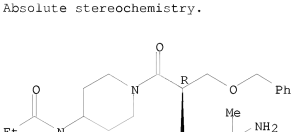
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and growth hormone releasing activity of heterocyclic dipeptide derivs.)

RN 185055-81-6 CAPLUS

CN Propanamide, 2-amino-2-methyl-N-[(1R)-2-oxo-2-[4-[(1-oxopropyl)phenylamino]-1-piperidinyl]-1-[(phenylmethoxy)methyl]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 83 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; R1 = H, alkyl, dialkylaminoalkylene; X = alkylene, alkylenecarbonyl, 5-6 membered N-containing heterocycle; R2 = aminocarbonyl, amino, (substituted) 5-6 membered N-containing heterocycle; R1R2 = atoms to complete a (substituted) 5-6 membered heterocycle; W1 = Ph; W2 = OH; or both W1, W2 = Me; X1 = H, Me; X2 = H, Me, MeOCH2; when both W1, W2 = Me, then X1 = Me and X2 = H], were prepared Thus, GE2270 factor A3 in DMF was treated with Et3N, DPPA, and serine (4-dimethylpiperidino)amide to give a condensation product which in THF was treated with Burgess reagent in CH2Cl2 followed by treatment with Me2CHOH and reflux to give I (NR1XR2 = 4-dimethylaminopiperidin-1-yl; W1 = Ph; W2 = OH; X1 = Me; X2 = MeOCH2). The latter had a min. inhibitory concentration of 0.5 μg/mL against Streptococcus pneumoniae L44.

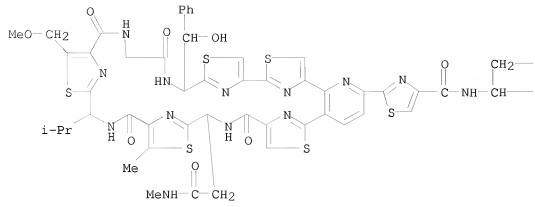
IT 182000-10-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of basic oxazolineamide derivs. of GE2270 and GE2270-like antibiotics)

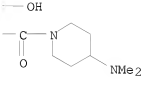
RN 182000-10-8 CAPLUS

CN 9H,16H-8,5:15,12:22,19:32,29:36,33-Pentanitrilo-5H,29H,33H-pyrido[3,2-al][1,11,18,25,31,4,7,14,21]pentathiatetraazacyclotetratriacontine-11-acetamide, 2-[4-[[[2-[4-(dimethylamino)-1-piperidinyl]-1-(hydroxymethyl)-2-oxoethyl]amino]carbonyl]-2-thiazolyl]-10,11,17,18,23,24,25,26,27,28-decahydro-28-(hydroxyphenylmethyl)-21-(methoxymethyl)-N,14-dimethyl-18-(1-methylethyl)-9,16,23,26-tetraoxo- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L6 ANSWER 84 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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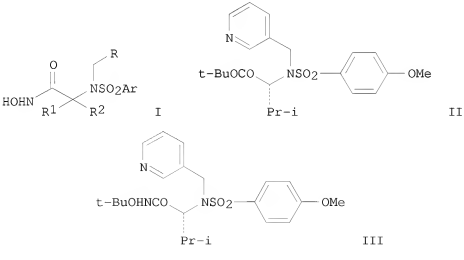
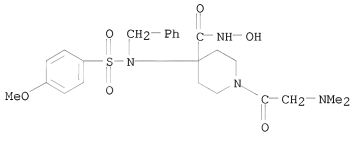


AB The title compds. [I; Ar = carbocyclic or heterocyclic aryl; R = H, alkyl, biaryl, etc.; R1 = H, alkyl, polyhalo alkyl, etc.; R2 = H, alkyl] and their salts, inhibitors of matrix-degrading metalloproteinase enzymes (stromelysin, collagenase and macrophage metalloelastase), were prepared and formulated. Reaction of N-(4-methoxybenzenesulfonyl)-D-valine tert-Bu ester with 3-picolyl chloride.HCl in the presence of K2CO3 in DMF followed by deesterification of the ester (R)-II, reaction of the corresponding acid.HCl with O-tert-butylhydroxylamine.HCl in the presence of 1-hydroxybenzotriazole, 4-methylmorpholine and N-(dimethylaminopropyl)-N'-ethylcarbodiimide.HCl in CH2Cl2 and treatment of the intermediate (R)-III with HCl in dichloroethane containing EtOH afforded (R)-I.HCl [Ar = 4-MeOC6H4; R = 3-pyridyl; R1 = isopropyl; R2 = H] which showed Ki of 17 nM against stromelysin.

IT 161314-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylsulfonamido-substituted hydroxamic acids as matrix-degrading metalloproteinase inhibitors)

RN 161314-09-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[2-(dimethylamino)acetyl]-N-hydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L6 ANSWER 85 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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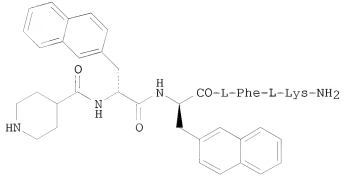


I

AB The present invention comprises growth hormone releasing peptides/peptidomimetics (GHRP) capable of causing release of growth hormone from the pituitary. Compns. containing the GHRP's of this invention are used to promote growth in mammals either alone or in combination with other growth promoting compds., especially insulin-like growth factor-1 (IGF-1).

In a method of this invention GHRP's in combination with IGF-1 are used to treat type II diabetes. Thus, I.CF3CO2H was prepared by standard solid-phase methods on an aminomethyl resin using 9-fluorenylmethoxycarbonyl (Fmoc) Nα protection. I induced significant body weight and organ weight gain in rats.

IT 179383-00-7P

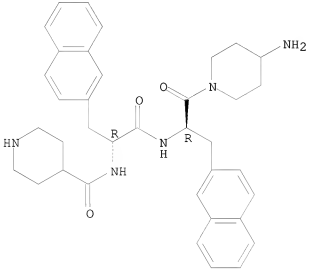
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of low mol. weight peptide mimics as growth hormone release stimulators)

RN 179383-00-7 CAPLUS

CN 4-Piperidinecarboxamide, N-[(1R)-2-[[(1R)-2-(4-amino-1-piperidinyl)-1-(2-naphthalenylmethyl)-2-oxoethyl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 86 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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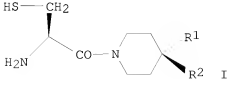


I

AB Chemotherapeutic compns. for treatment of cancer contain substituted piperidine analogs (I; R1 = COR, CO2R, CONHR, OH, OCOR, CN, CH2OR, NHCOR,

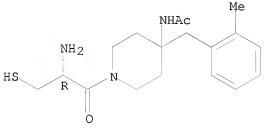
NHSO2R, etc.; R = alkyl, aryl; R2 = aryl, aralkyl, heterocycle, heteroaralkyl, etc.) as inhibitors of farnesyl-protein transferase (FTase) and farnesylation of the oncogene protein Ras.

IT 177990-08-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(piperidine analogs as inhibitors of farnesyl-protein transferase for treatment of cancer)

RN 177990-08-8 CAPLUS

CN Acetamide, N-[1-(2-amino-3-mercapto-1-oxopropyl)-4-[(2-methylphenyl)methyl]-4-piperidinyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 87 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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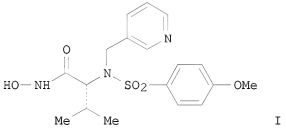


I

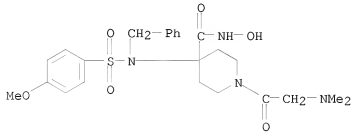
AB The invention relates to a method of inhibiting metalloelastase activity, of inhibiting the degradation of elastin, or of treating macrophage metalloelastase dependent conditions in mammals which comprises administering to a mammal in need thereof an effective macrophage metalloelastase inhibiting amount of (HO)NHCOCR1R2N(CH2R)SO2Ar wherein: Ar is carbocyclic or heterocyclic aryl; R is, e.g., H, lower alkyl, carbocyclic aryl-lower alkyl; R1 is, e.g., H, lower alkyl, carbocyclic aryl-lower alkyl; R2 = H or lower alkyl, or of a pharmaceutically acceptable prodrug derivative thereof, or of a pharmaceutically acceptable salt thereof, or of pharmaceutical compns. comprising a said compound Thus, e.g., treatment of D-valine with 4-methoxybenzenesulfonyl chloride followed by esterification with N,N-dimethylformamide di-t-Bu acetal afforded N-[4-methoxybenzenesulfonyl]-D-valine t-Bu ester; treatment of the latter with 3-picolyl chloride hydrochloride followed by HCl afforded 2(R)-[[4-methoxybenzenesulfonyl](3-picolyl)amino]-3-methylbutanoic acid hydrochloride; coupling with O-t-butylhydroxylamine hydrochloride followed by HCl afforded N-hydroxy-2(R)-[[4-methoxybenzenesulfonyl](3-picolyl)amino]-3-methylbutanamide.xHCl (I.xHCl) which inhibited stromelysin (based on its hydrolysis of Substance P) with Ki = 17 nM,

inhibited stromelysin (based on human aggrecan substrate) with IC50 = 55 nM, inhibited collagenase with Ki = 62 nM, and inhibited the degradation of [3H]elastin by mouse macrophage metalloelastase with an IC50 of about 8 nM. Pharmaceutical formulations were given.

IT 161314-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(arylsulfonamido-substituted hydroxamic acids and method of inhibiting metalloelastase activity, inhibiting elastin degradation, or treating macrophage metalloelastase dependent conditions in mammals)

RN 161314-09-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[2-(dimethylamino)acetyl]-N-hydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L6 ANSWER 88 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

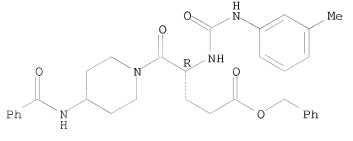
AB The development of a novel series of carbamoylamine acid benzoylpiperidides as CCKB ligands is described. Selected members of the series antagonized CCK8-induced calcium mobilization and showed efficacy in the mouse elevated-plus maze, a measure of potential anxiolytic activity.

IT 173987-01-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of amino acid-derived piperidides as CCK antagonists)

RN 173987-01-4 CAPLUS

CN 1-Piperidinepentanoic acid, 4-(benzoylamino)-γ-[[[(3-methylphenyl)amino]carbonyl]amino]-δ-oxo-, phenylmethyl ester, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 89 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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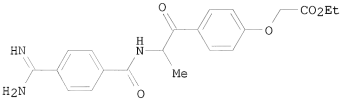


I

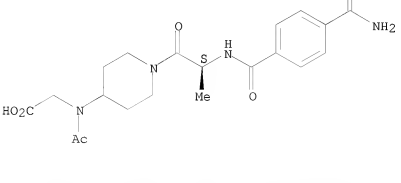
AB LCOMZCH2COT [L = ACOZ1CH(G), ACH2Z2CH(G), ANHCOCH(G), etc.; A = aryl or cycloalkylalkyl groups Q1,Q2, etc.; D = (CH2)1-4, (CH2)0-3O; G = H, amino acid side chain; M = 1,4-piperidinylene, (un)substituted 1,4-phenylene; R = R1NHC(:NR2), R1NHCH2, etc.; R1,R2 = H, alkyl, alkoxy, etc.; R1R2 = atoms to complete a 5,5-dimethyl- or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl group; T = NH2, OH, alkoxy, etc.; 1 of X,Y = CH and the other = CH, N, etc.; Z = O, CH2, NH, etc.; Z1 = (alkyl- or alkoxycarbonyl-substituted) CH2, (alkyl)imino, etc.; Z2 = O, (acyl)imino; m,n = 0-5] were prepared Thus, (S)-4-(HO)C6H4COCHMeNHCO2CMe3 was etherified by BrCH2CO2Et and the deprotected product N-acylated by 4-[H2N(Me3CMe2SiON:)C]C6H4CO2H to give, after deprotection, title compound (S)-I which had ED50 of 0.2mg/kg orally in mice for production of plasma capable of inhibiting aggregation of human platelet-rich plasma.

IT 170095-03-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenoxyacetic acid derivs. and analogs as cell adhesion inhibitors)

RN 170095-03-1 CAPLUS

CN Glycine, N-acetyl-N-[1-[2-[[4-(aminoiminomethyl)benzoyl]amino]-1-oxopropyl]-4-piperidinyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 90 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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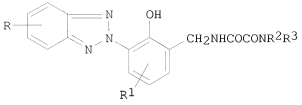

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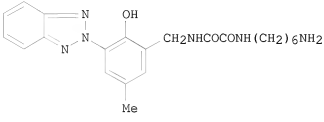


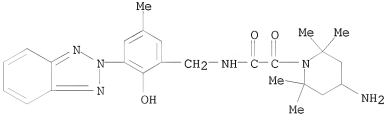
II

AB Title compds. [I; R = H, Cl, Br, (substituted) aliphatyl, alkoxy, alkoxycarbonyl, alkylaminocarbonyl, alkoxysulfonyl, CO2H, CONH2, SO3H, etc.; R1 = H, Cl, Br, (substituted) aliphatyl, aryl, araliphatyl, alicyclyl, alkoxy, alkylaminocarbonyl, etc.; R2 = H, (substituted) aliphatyl, araliphatyl, alicyclyl; R3 = H, (substituted) aliphatyl, alicyclyl, araliphatyl, aryl, (aromatic) heterocyclyl, etc.], were prepared Thus, 1,6-hexanediamine in MeOH was treated with Et N-[2-hydroxy-3-(2H-benzotriazol-2-yl)-5-methylbenzyl]oxamate (preparation given) at 55°; the mixture was refluxed 2 h to give 93% title compound II. Polycarbonate bars containing I placed in a QUV accelerated weathering tester showed a YID (yellowness index) of 20-30 after 45 days, vs. a YID of 50 for untreated controls.

IT 163295-10-1P
RL: MOA (Modifier or additive use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(preparation of, as UV absorber for stabilization of polymers)

RN 163295-10-1 CAPLUS

CN 1-Piperidineacetamide, 4-amino-N-[[3-(2H-benzotriazol-2-yl)-2-hydroxy-5-methylphenyl]methyl]-2,2,6,6-tetramethyl-α-oxo- (CA INDEX NAME)



L6 ANSWER 91 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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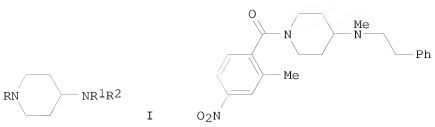
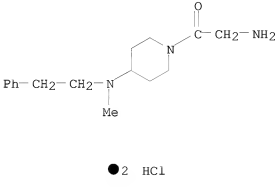


AB Title compds. [I; R = substituted Bz, (un)substituted carbamoyl, etc.; R1 = H, (hydroxy)alkyl; R2 = (un)substituted phenyl(oxy)alkyl; NR1R2 = (un)substituted pyrrolidino, -piperidino, morpholino, -1,2,3,4-tetrahydroisoquinolino] were prepared Thus, title compound II gave 24.0mL/min increase in femoral artery blood flow at 10-30μL of a 100nM solution intra-arterially in dogs.

IT 167623-63-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-benzoylpiperidine-4-amines as peripheral vasodilators)

RN 167623-63-4 CAPLUS

CN Ethanone, 2-amino-1-[4-[methyl(2-phenylethyl)amino]-1-piperidinyl]-, hydrochloride (1:2) (CA INDEX NAME)



L6 ANSWER 92 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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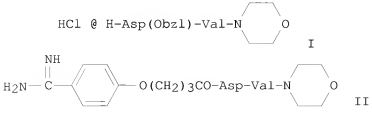


AB Peptides R1(O)mA1CO(A2)nNHCHR2CONHA3R3 (R1 = aryl which may have one or

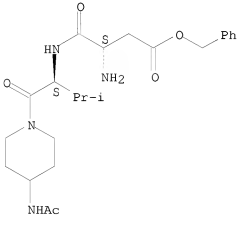
more suitable substituents; R2 = optionally protected lower carboxyalkyl; R3 = a carboxamide group; A1 = lower alkylene; A2 = NR4CH2CO or NHR4HCO; R4 = lower alkyl; A3 = lower alkylene which may have one or more substituents; m, n = 0, 1), useful as antithrombotics, antiinflammatories, and platelet aggregation inhibitors and for the treatment of disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura, essential blood platelet disease, immune diseases, and thrombus formation during transplants, circulation outside the body, blood vessel surgery, and replacement of heart valves, and restenosis and/or reinfarction of blood vessel, are prepared Thus, dipeptide (I) was acylated by 4-[4-(N-benzyloxycarbonylamidino)phenoxy]butyric acid in the presence of 1-hydroxy-1H-benzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide in DMF at -20° to room temperature followed by hydrogenolysis over 10% Pd-C in aqueous 1 N HCl/THF and HPLC purification to give
title peptide (II.CF3CO2H). II.CF3CO2H was orally administered to a beagle dog; after 1 h blood sample was taken and platelet rich plasma prepared from the blood sample inhibited 96% the ADP-induced blood platelet coagulation.

IT 160139-78-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with phenoxybutyric acid derivative)

RN 160139-78-6 CAPLUS

CN Butanoic acid, 4-[[1-[[4-(acetylamino)-1-piperidinyl]carbonyl]-2-methylpropyl]amino]-3-amino-4-oxo-, phenylmethyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 93 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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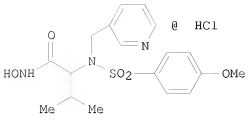


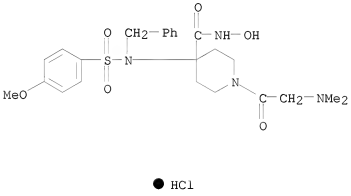
I

AB The title compds. OHNHCOC(R1)R2N(CH2R)SO2A [A = carbocyclic aryl, heterocyclic aryl; R = H, (un)substituted alkyl, aryl, biaryl, etc.; R1 = H, lower alkyl, aryl, biaryl, etc.; R2 = H, lower alkyl; R1R2 may form a heterocyclic substituent for cycloalkane substituent], which are effect as matrix metalloproteinase inhibitors (no data) useful in the treatment of arthritis (no data), are prepared Thus, arylsulfonamido-substituted hydroxamic acid I, m.p. 169-170° (decomposition), was prepared from N-(tert-butyloxy)-2(R)-[[4-methoxybenzenesulfonyl](3-picolyl)amino]-3-methylbutanamide and HCl.

IT 161314-09-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antiinflammatory agent)

RN 161314-09-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[2-(dimethylamino)acetyl]-N-hydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L6 ANSWER 94 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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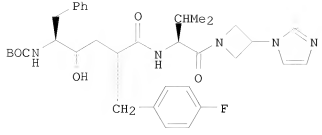


I

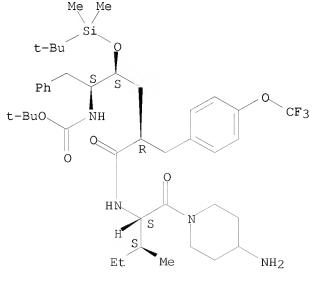
AB R1(CR5CR6)nO2CNHCHR2CH(OH)CH2CHR3CONHCHR4COX(CR7CR8)mX [R1 = alkyl, cycloalkyl, aryl, heterocyclyl, carbamoyl; R2 = alkyl, cycloalkylalkyl, arylalkyl, heterocyclylalkyl; R3 = alkyl, cycloalkyl, cycloalkylalkyl, arylalkyl, arylalkenyl, heterocyclylalkyl, heterocyclylalkenyl; R4 = alkyl, cycloalkyl, aryl, heterocyclyl; R5-R8 = H, alkyl, cycloalkyl; R5R6, R7R8 = atoms to form 3-8 membered carbocyclic rings; X = (substituted) mono- or bicyclic heterocyclyl; N, m = 0-2; alkyl or cycloalkyl groups may be partially or fully fluorinated], were prepared Thus, title compound I was prepared by solution phase methods. Title compds. showed IC100 = 0.1-10 μg/mL againsts HIV-1 in C8166 cells.

IT 158655-22-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for peptide derivative retroviral protease inhibitor)

RN 158655-22-2 CAPLUS

CN Carbamic acid, [5-[[1-[(4-amino-1-piperidinyl)carbonyl]-2-methylbutyl]amino]-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-oxo-1-(phenylmethyl)-4-[[4-(trifluoromethoxy)phenyl]methyl]pentyl]-, 1,1-dimethylethyl ester, [1S-[1R*,2R*,4S*,5(1R*,2R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 95 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

AB The title compds. R1(CR9R10)nO2CNHCR2HC(OH)HCH2CR3HCONHCR4HCOX(CR11R12)mNR5R6 [R1 = C1-6 alkyl, C3-8 cycloalkyl, aryl, heterocyclyl, etc.; R2 =

(un)substituted alkyl; R3 = (un)substituted alkyl, C3-8 cycloalkyl, (un)substituted alkenyl, etc.; R4 = C1-6 alkyl, C3-8 cycloalkyl, aryl, heterocyclyl; R5, R6 = H, (un)substituted C1-6 alkyl, C3-7 cycloalkyl, etc.; R9, R10 = H, C1-6 alkyl, C3-8 cycloalkyl, etc.; X = 4-10-membered mono- or bicyclic heterocyclic divalent residue containing 1 ring N through which the group is attached to the adjacent CO group; m, n = 0-2], inhibitors of retroviral proteases (no data) and useful in the treatment and prophylaxis of human retroviral infections such as AIDS (no data), are prepared Thus, 1-[N-[(R)-2-benzyl-(S)-5-tert-butoxycarbonylamino-(S)-4-hydroxy-6-phenylhexanoyl]-(S)-valyl]-4-methylaminopiperidine was prepared from 1-[N-tert-butoxycarbonyl-(S)-valyl]-4-dimethylaminopiperidine in 5 steps.

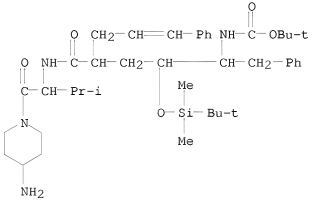
IT 155456-11-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and intermediate in preparation of heterocyclic retroviral protease inhibitors and antiviral agents)

RN 155456-11-4 CAPLUS

CN Carbamic acid, [4-[[[1-[(4-amino-1-piperidinyl)carbonyl]-2-methylpropyl]amino]carbonyl]-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-phenyl-1-(phenylmethyl)-6-heptenyl]-, 1,1-dimethylethyl ester, [1S-[1R*,2R*,4S*(R*)]]- (9CI) (CA INDEX NAME)



L6 ANSWER 96 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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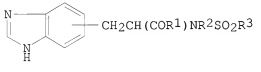


I

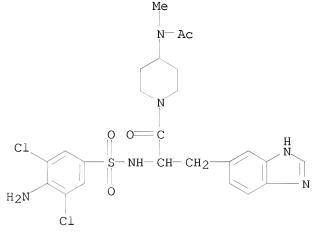
AB Title compds. [I; R1 = (Ph-substituted) dialkylamino, (substituted) pyrrolidino, piperidino, hexamethylenimino, etc.; R2 = H, alkyl; R3 = (substituted) Ph, naphthyl, indanyl, quinolyl, 1,2,3,4-tetrahydroquinolyl, isoquinolyl, carbazotyl, dibenzofuryl, etc.], were prepared Thus, 4-nitrophenylalanine was converted in several steps to 4-amino-3-nitrophenylalanyl 4-methylpiperidineamide. This in CH2Cl2 containing ET3N was condensed with 4-amino-3,5-dichlorobenzenesulfonyl

chloride and the product was hydrogenated in HCO2H over Pd/C to give 4-amino-N-[1-(1H-benzimidazol-5-ylmethyl)-2-(4-methylpiperidin-1-yl)-2-oxoethyl]-3,5-dichlorobenzenesulfonamide. I showed ED200 of 1.7 - 9.2 μM in a test of thrombin-induced blood coagulation.

IT 152134-73-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antithrombotic)

RN 152134-73-1 CAPLUS

CN Acetamide, N-[1-[2-[[(4-amino-3,5-dichlorophenyl)sulfonyl]amino]-3-(1H-benzimidazol-6-yl)-1-oxopropyl]-4-piperidinyl]-N-methyl- (CA INDEX NAME)



L6 ANSWER 97 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN

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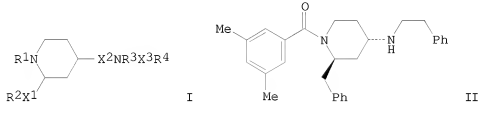
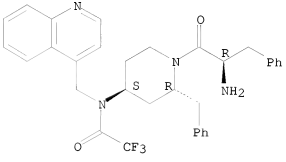


AB Title compds. [I; R1 = (substituted) aralkyl, aryloxyalkyl, aroyl, arylcarbamoyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, aralkoxycarbonyl, α-araminoacid ocyl residue, etc.; R2 = cycloalkyl, (substituted) (hetero)aryl; R3 = H, alkyl carbamoyl, (substituted) alkanoyl, alkenoyl; (R4 = (substituted) aryl, (partially hydrogenated) heteroaryl; X1 = (H2, CH2CH2, bond, (ketalized) CO, (etherified) HOCH; X2 = alkylene, CO, bond; X3 = CO, oxoalkylene, oxoazaalkylene, hydroxyalkylene, etc.], were prepared Thus, Et (R)-3-amino-4-phenylbutyrate was converted to (2R, 4RS)-2-benzyl-1-(3,5-dimethylbenzoyl)-4-piperidineamine in several steps and the latter was stirred with PhCH2CHO, NaOAc, HOAc, and NaBH3CN in MeOH to give title compound II and its diastereomer. I inhibited substance P-induced blood vessel dilation in guinea pig ears beginning at 0.01 mg/kg i.v.

IT 150708-36-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of, as intermediate for substance P antagonist)
RN 150708-36-4 CAPLUS
CN Acetamide, N-[1-(2-amino-1-oxo-3-phenylpropyl)-2-(phenylmethyl)-4-piperidinyl]-2,2,2-trifluoro-N-(4-quinolinylmethyl)-, [2R-[1(R*),2α,4β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 98 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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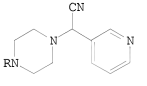
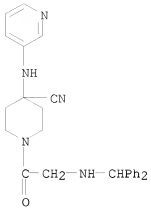


AB A series of (pyridylcyanomethyl)piperazines, e.g., I [R = Bz, PhCH2CO, PhCH2CH2CO, Ph(CH2)3CO, PhCH:CHCO, BuCO, Ph2CHCO, Ph2CHCH2CO, Ph2CHNHCH2CO, Ph2CHCONHCH2CO, Ph2CHCH2CO2] was prepared and evaluated for PAF-antagonist activity. Compds. were tested in vitro in a PAF-induced platelet aggregation assay and in vivo in a PAF-induced hypotension test in normotensive rats. Oral activity was ascertained through a PAF-induced mortality test in mice. The main structure-activity trends of the series were established. Activity was mainly found in four skeletons: 1-acyl-4-(3-pyridylcyanomethyl)piperazine, 1-acyl-4-(4-pyridylcyanomethyl)piperazine, 1-acyl-4-(3-pyridylcyanomethyl)piperidine, and 1-acyl-4-cyano-4-(3-pyridylamino)piperidine. The acyl substituents, diphenylacetyl and 3,3-diphenylpropionyl, provided the most active compds., and the introduction of an amine or hydroxy group in the 3,3-diphenylpropionyl substituent led to further improvement in oral activity. As a result, three of the most active compds. I [R = Ph2CH(CH2)2NHCOCH2, Ph2CHNHCH2CO, Ph2C(OH)CH2CO] have been selected for further pharmacol. development.
IT 143817-27-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and PAF antagonists activity of)
RN 143817-27-0 CAPLUS
CN 4-Piperidinecarbonitrile, 1-[2-[(diphenylmethyl)amino]acetyl]-4-(3-pyridinylamino)- (CA INDEX NAME)



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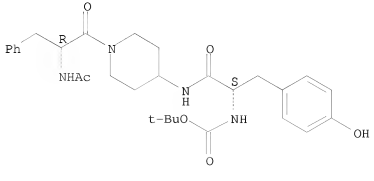
GI For diagram(s), see printed CA Issue.
AB In order to test the theory that high μ-activity of opioid peptides could be elicited by the presence of an amino-terminal L-Tyr residue and a Phe aromatic ring held in the proper relative spatial disposition, a novel series of hybrid retro peptides, I and II, were prepared in which L-Tyr was linked to N-acyl Phe through a variety of diamine spacers. These compds. were evaluated for opioid agonist and antagonist activity in the guinea pig ileum in vitro assay. Analogs containing a 1,2-ethanediamine spacer, which conferred a Tyr-Phe separation distance closest to that found in Phe3 opioid peptides, were more potent agonists than the corresponding analogs containing a 1,3-propanediamine spacer. Agonist activity was observed for both L-Phe and D-Phe analogs, consistent with the known activity for both Phe stereochemistries for certain Phe3 opioid peptide analogs. Concerning the diamine spacer, conformational constraints imposed by 4-aminopiperidine and 4-(aminomethyl)piperidine as well as the presence of a hydroxyl group eliminated activity, but the presence of gem-di-Me substitution next to the nitrogen attached to Tyr increased activity substantially for the D-Phe derivative
IT 120687-47-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
RN 120687-47-0 CAPLUS
CN Carbamic acid, [2-[[1-[2-(acetylamino)-1-oxo-3-phenylpropyl]-4-piperidinyl]amino]-1-[(4-hydroxyphenyl)methyl]-2-oxoethyl]-, 1,1-dimethylethyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 100 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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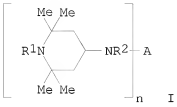


I

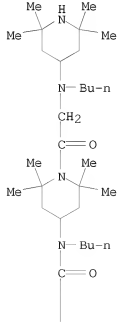
AB Piperidinylhydrocarbylamines I (R1 = H, O, OH, NO, CH2CN, C1-8 alkyl, allyl, benzyl, OH-monosubstituted C2-4 alkyl; C1-18 alkyloxy or C1-8 acyl; R2 = hydrocarbyl or tetramethylpiperidinyl; n = 1 or 2, where n = 1 then A = piperidinylaminoalkylenecarbonyl derivative and if n = 2 then A = various carbonylalkyleneaminoalkylenecarbonyl derivs.). A mixture of polypropylene (melt index 3 g/10 min) 1000, I 1, tris(2,4-di-tert-butylphenyl)phosphite 0.5, pentaerythritol tetrakis[3,5-di-tert-butyl-4-hydroxyphenyl)propionate 0.5, and Ca stearate 1 g was extruded and blow molded to give a 50-μm-thick film having time for 50% decrease in tenacity in weatherometer 2840 h, vs. 380 h without I.

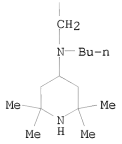
IT 120215-43-2
RL: USES (Uses)
(stabilizer, for polyolefin and organic compds.)

RN 120215-43-2 CAPLUS

CN Acetamide, N-butyl-2-[butyl(2,2,6,6-tetramethyl-4-piperidinyl)amino]-N-[1-[2-[butyl(2,2,6,6-tetramethyl-4-piperidinyl)amino]acetyl]-2,2,6,6-tetramethyl-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A





L6 ANSWER 101 OF 102 CAPLUS COPYRIGHT 2010 ACS on STN
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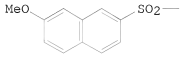
Q=



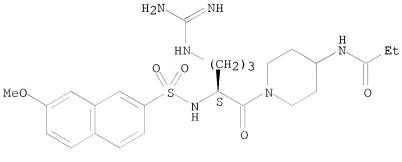
AB HN:C(NH2)NH(CH2)3CH(NHR1)COR2[I, R1 = substituted naphthyl(alkyl), substituted heterocyclyl(alkyl); R2 = (substituted) heterocyclyl, substituted amino, morpholinocarbonyl], useful as trypsin inhibitors, were prepared Thus, treatment of 1-(NG-nitro-L-arginyl)-4-(N-isopropyl)piperidinecarboxamide-HCl with QCl in DMF containing Et3N at room temperature for 2 h gave 58% 1-[N2-(7-methoxy-2-naphthylsulfonyl)-NG-nitro-L-arginyl]-4-(N-isopropyl)piperidinecarboxamide, whose hydrogenolysis over Pd/C gave 63% I [R1 = Q, R2 = 4-(isopropylcarbamoyl)-1-piperidinyl].

IT 102125-55-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as trypsin inhibitor)

RN 102125-55-3 CAPLUS

CN Propanamide, N-[1-[5-[(aminoiminomethyl)amino]-2-[[(7-methoxy-2-naphthalenyl)sulfonyl]amino]-1-oxopentyl]-4-piperidinyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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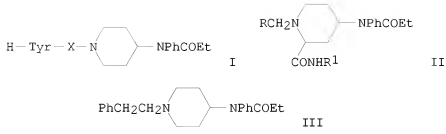
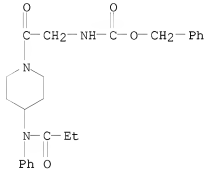


AB Title analogs I (X = null, Gly, Gly-Gly), cis-II [R = CH2Ph, R1 = H; R = Me, R1 = (CH2)nPh (n = 1, 2, 3, 4), CH2CONHCH2CH2Ph], and trans-II (R = H, R1 = CH2Ph) were prepared in order to investigate whether or not fentanyl (III) and enkephalins interact with common subsites on opioid receptors. The design of the analogs was based on the possibility of structural analogy between the two aromatic rings of III and the Tyr1 and Phe4 residues of the opioid peptides. The synthesized compds. showed very weak or no opioid activity as tested in the elec. stimulated longitudinal muscle of the guinea pig ileum or mouse vas deferens prepns. Apparently, III and the opioid peptides interact with different subsites on either μ or δ receptors. Studies using the irreversible μ opioid receptor antagonist, β-funaltrexamine, indicate that III interacts preferentially with μ opioid receptors.

IT 85221-28-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 85221-28-9 CAPLUS

CN Carbamic acid, [2-oxo-2-[4-[(1-oxopropyl)phenylamino]-1-piperidinyl]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST	465.53	658.78

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